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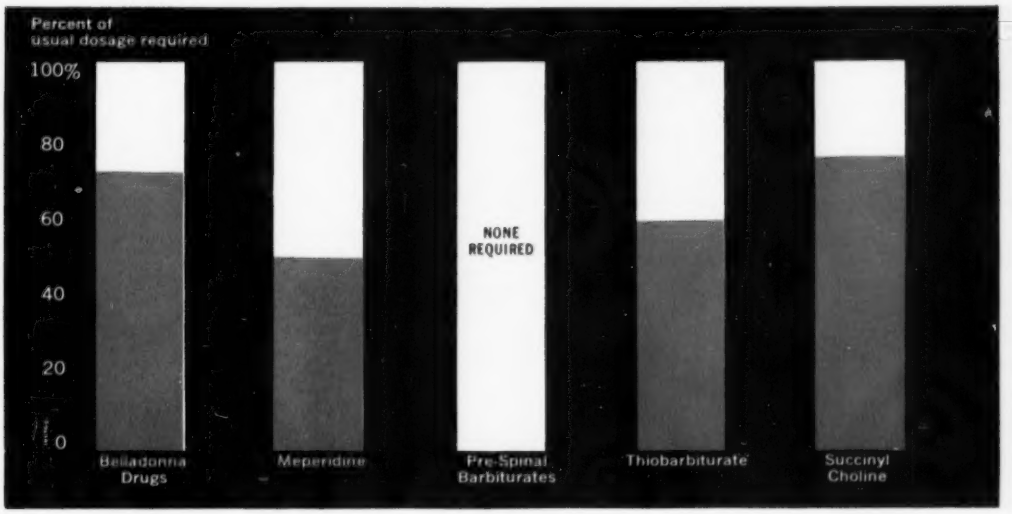

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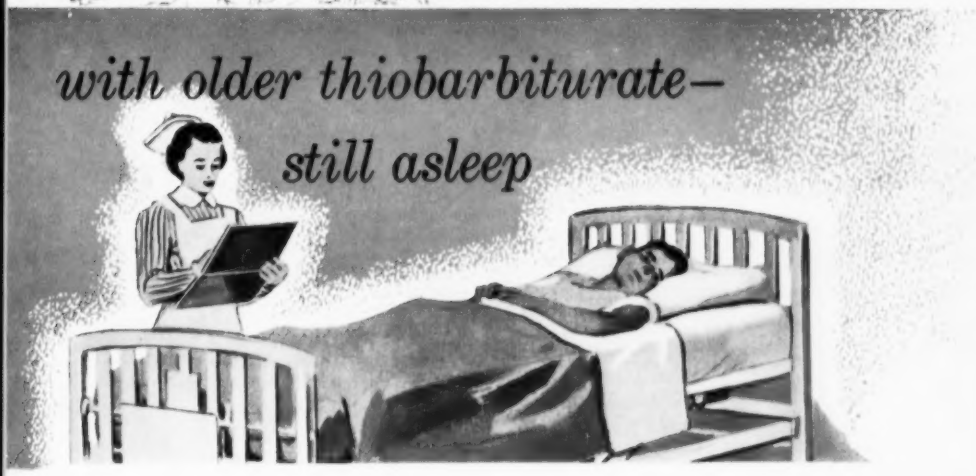

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SURGERY

Histochemical Characterization of Heart and Skeletal Muscle During Growth

PETER V. MOULDER, M.D., LILLIAN EICHELBERGER, Ph.D., and MICHAEL ROMA, Chicago

Contemporary events have greatly stimulated investigation of the physiology and biochemistry of the heart, as well as increasing interest in cardiac surgery and congenital and coronary artery disease.

Analytical electrolyte data on the heart are voluminous, but little is to be found on the complete histochemical characterization of this tissue.[1] In fact, almost nothing has been done histochemically on the canine heart, the commonest source of cardiac research.

Histochemical changes in various parts of the heart following experimental coronary artery occlusion in both young and adult dogs have been studied by Hastings, Blumgart, Lowry, and Gilligan,[2] and Lowry et al.[3] Their analytical data were expressed on a fat-free, blood-free basis; their calculated data were made using an assumed value for the connective tissue mass. We have actually determined the connective tissue mass for all of the tissues presented here. Brodie [4] did histochemical studies on a variety of tissues, including the myocardium of a small number of dogs.

Submitted for publication Dec. 14, 1956.

From the Departments of Surgery and Biochemistry, University of Chicago, the School of Medicine.

This investigation was aided in part by research grants from the Home for Destitute Crippled Children and the Oscar Mayer Foundation for Cardiovascular Research.

Extensive studies also have been made on the histochemical characterization of skeletal muscle taken from adult dogs. An excellent discussion of this work has been made by Manery [1] in a recent review. Data on skeletal muscle of a group of young puppies also appeared recently.[5]

Age causes considerable variation of histochemical balance in many tissues. It has been found convenient to use the puppy life span as a general indicator of this major variable. Myocardium being uniquely always active, it might be anticipated that some differential from the episodically active skeletal muscles would be found. With this in mind, comparative data will be shown for cardiac and skeletal muscle taken simultaneously from 11 normal puppies apportioned into two age groups. These findings clarify the normal histochemistry of the different muscles in the different age groups and may provide a basis for further comparative studies in the same direction under abnormal conditions.

Experimental Procedures

The puppies used in this study were whelped and maintained in metabolism cages in a special isolated puppy room throughout their life span. They were weaned at 8 weeks of age and were given a diet of Rival dog food with milk supplement. They were fed at definite intervals of time during the day throughout their growth period. At the desired age, the animals were anesthetized with pentobarbital (Nembutal) and 50 ml. of blood was removed from the femoral artery, of which

approximately 35 ml. was collected under oil for serum analyses and 15 ml. was defibrinated for the whole-blood analyses. Immediately following, the thigh muscles were removed, after which the beating heart was quickly taken. The tissues were wiped slightly with dry gauze and placed at once into ground-glass-stoppered jars. The jars were placed in a refrigerator overnight, and, after all visible fascia, connective tissue, and fat were trimmed from the cold specimens, they were quickly placed into glass-stoppered weighing bottles and minced with the sharp points of scissors. The handling was executed with speed at all times to minimize water loss. Aliquot samples of the minced tissues were weighed for all analyses.

The serum was analyzed for water, chloride, sodium, potassium, calcium, magnesium, and total nitrogen. Whole defibrinated blood was analyzed for cell volume, water, chloride, sodium, and potassium. The cardiac and thigh muscle samples were analyzed for water, fat, residual blood, chloride, sodium, potassium, calcium, magnesium, total nitrogen, and collagen nitrogen.

Serum and Whole Blood Analyses

The serum and whole-blood chloride were measured by the method of Van Slyke with the Wilson and Ball modification.[6] Sodium and potassium were determined on the Perkin-Elmer Flamephotometer; serum calcium, by the method of Kramer and Tisdall[7]; magnesium, by the method of Denis,[8] the amount of magnesium being estimated from the spectrophotometric determination of phosphate by the Gomori[9] method, and total nitrogen, as described by Campbell and Hanna.[10] The content of water in serum and blood was made by drying 1 ml. portions in a 100 C oven. Blood cell volume was estimated by the use of Van Allen hematocrit tubes without anticoagulant.[11] The concentration of the constituents of the red blood cells was calculated indirectly from the values for whole blood and serum and the cell volume.

Since the chemical methods for the analyses of the tissues were reported in detail in a recent publication from this laboratory,[5] they will not be repeated here. As before, the tissue data are calculated on a fat-free, blood-free basis. The amount of circulatory space of the blood in the thigh and heart muscle was determined by the spectrophotometric comparison of the amount of hemoglobin in the tissue with that of the whole blood taken simultaneously. This method has been given in detail in a previous paper.[12]

Having determined the volume of residual blood per kilogram of tissue, corrections for the constituents in this volume can easily be made.

Calculations

In this study of heart muscle we shall follow the considerations set forth in our previous paper for skeletal muscle, that is, that the extracellular compartment (F) of a muscle consists of connective tissue solids and extracellular fluid, and the intracellular compartment (C) consists of protein solids and water. Throughout the presentation of the data, parentheses ( ) represent milliequivalents or grams per kilogram of tissue; brackets [ ] represent milliequivalents or grams per kilogram of water, and braces { } represent milliequivalents or grams per kilogram of phase.

In brief, from the chloride values, the mass of extracellular fluid was calculated, and from the collagen nitrogen values the weight of the connective tissue solids was estimated. The mass of the intracellular compartment per kilogram of muscle was then obtained by subtracting the total extracellular mass from 1000.

Ionic concentrations in the extracellular fluid water were derived from the serum concentration and the Gibbs-Donnan distribution ratio. The factor of 0.95 was used for chloride, sodium, and potassium for the heart, as well as the skeletal muscle. Based on the observations of Drinker et al.[13] on the composition of cardiac lymph, Lowry, Gilligan, and Hastings used a ratio value of 0.98 for heart muscle. The use of either of these factors makes little difference in the final estimations. For calcium and magnesium we have used the equations projected by Manery[1]:

$$\sqrt{[Ca]_F}/\sqrt{[Ca]_s}=0.714;$$

$$\sqrt{[Mg]_F}/\sqrt{[Mg]_s}=0.867$$

The equations used in the calculation of the (F) phases follow: The (F) phase consists of the connective tissue solids $(F)_s$ + the ultrafiltrate $(F)_U$, or $(F)=(F)_s+(F)_U$.

$$(F)_s=(\text{collagen N})_M/15.8\times 100$$

where 15.8 represents the grams of collagen nitrogen indicating 100 gm. of connective tissue solids. $(F)_U=(Cl)_M/\{Cl\}_F\times 1000$; $\{Cl\}_F=0.99/0.95\times[Cl]_s$. 0.99 is taken as the water concentration in the extracellular phase in grams of water per gram of fluid.

To calculate the concentration of water in the intracellular phase, $\{H_2O\}_C$=grams of intracellular water per kilogram of muscle $(H_2O)_C$ divided by the total intracellular phase (C), or $\{H_2O\}_C=(H_2O)_C/(C)$.

The concentration of the individual cations in the muscle fibers was calculated after correcting for the concentration of the constituent found in the extracellular compartment. Since the extracellular compartment consists of the ultrafiltrate phase plus the connective tissue solids, separate calculations were made for the amount of the individual cation associated with each of the phases

in the compartment. To calculate the amounts of the constituents associated with the connective tissue solids, we have used the data of previous studies on dog tendon[14] and have used the basic assumption that the connective tissue of cardiac and skeletal muscle resembles all other connective tissue in water, nitrogen, and electrolyte concentrations and also that the collagen nitrogen delineates the connective tissue weight. One hundred grams of tendon solids was found to be associated with 157 gm. of water, 17.2 gm. of total nitrogen; 15.8 gm. of collagen nitrogen; 20.65 mEq. of chloride, and 20.2 mEq. of sodium. From the data of Manery, Danielson, and Hastings[15] a value of 3.4 mEq. was used for potassium. Since the amounts of calcium and magnesium in tendon solids have not been determined, we could not estimate these corrections and could only correct for the amounts in the ultrafiltrate water.

The amounts of calcium and magnesium in the extracellular water were obtained by multiplying their respective concentrations in the ultrafiltrate by the volume of the extracellular water per kilogram of muscle. After subtracting this amount from the total amounts found in a kilogram of tissue, the remaining amount must be allocated to some other place, possibly the muscle fibers.

More precisely, however, the amounts of potassium and sodium in the extracellular phase were obtained by calculating the amount in the ultrafiltrate volume and the amount associated with the connective tissue solids. After subtracting the sum of these two amounts, $(K)_F$ and $(Na)_F$, respectively, from the total amounts, $(K)_M$ and $(Na)_M$, the remaining quantity must be allocated to the cells. The concentration of potassium can then be calculated per kilogram of muscle cells $\{K\}_C$, or per kilogram of intracellular water $[K]_C$.

Results

The original data for blood, heart muscle, and skeletal muscle are collected into two groups, arranged according to age. In Table 1 are presented the values in detail for three representative puppies, together with the average mean values with standard deviations for Group I, consisting of five puppies, 78-124 days of age.

In Table 2 are the average analytical data with standard deviations for Group II, consisting of six puppies, 142-218 days of age. Again, three representative puppies are given for illustrative purposes.

In considering these original data, two types of comparisons are made: first, comparisons of the tissue findings of one group with those of the other group, and, second, comparisons of the tissue values for the myocardium with those of the skeletal muscle. The serum and blood values vary insignificantly from one group to the other. When the myocardium is considered, the water content, potassium, magnesium, and

TABLE 1.—*Original Data: Electrolyte and Water Content of Serum, Blood, Heart, and Thigh Muscles from Puppies During Growth* *

	Water	Cl	Na	K	Ca	Mg	Total N	Collagen N
	Gm.	mEq.	mEq.	mEq.	mEq.	mEq.	Gm.	Gm.
Group I: 5 puppies, ages 87-124 days								
Puppy W 11, 87 days old								
Serum	926	109.6	144.2	4.82	5.20	1.86	8.64	
Blood	820	88.4	125.7	6.16				
Heart	794	36.9	38.9	74.3		14.2	28.4	3.8
Thigh	803	35.0	39.2	82.0	2.17	15.4	28.5	7.2
Puppy W 20, 119 days old								
Serum	934	117.5	149.0	4.62	5.70	1.75	8.12	
Blood	813	91.3	132.0	6.24				
Heart	802	35.4	41.6	79.4	1.73	16.7	27.9	5.2
Thigh	796	27.5	34.1	88.0	1.75	15.6	31.2	7.0
Puppy W 12, 120 days old								
Serum	928	113.5	147.5	4.62	5.15	2.09	8.31	
Blood	803	87.8	131.0	5.98				
Heart	803	37.2	40.3	77.7	1.98	15.6	25.4	5.9
Thigh	788	28.6	34.0	92.3	1.97	16.5	28.3	8.8
Means for Group								
Serum	929	113.2	146.9	4.71	5.47	1.93	8.31	
S.D.†	3	3.4	1.9	0.28	0.21	0.21	0.37	
Blood	814	88.9	128.9	6.24				
S.D.	6	2.4	2.5	0.28				
Heart	804	36.7	34.0	90.2	1.93	16.3	27.1	5.1
S.D.	6	0.8	2.2	4.5	0.14	1.3	1.2	0.5
Thigh	796	29.1	34.0	90.2	1.93	16.3	29.6	7.1
S.D.	5	3.5	2.4	4.5	0.14	0.9	1.1	1.0

* Units are expressed per kilogram of blood-free, fat-free tissue.
† S.D.=standard deviation.

TABLE 2.—*Original Data: Electrolyte and Water Content of Serum, Blood, Heart, and Thigh Muscles of Puppies During Growth* *

	Water	Cl	Na	K	Ca	Mg	Total N	Collagen N
	Gm.	mEq.	mEq.	mEq.	mEq.	mEq.	Gm.	Gm.
Group II: 6 puppies, ages 142–218 days								
Puppy W 14, 142 days old								
Serum	926	113.5	147.0	4.56	5.58	2.21	8.56	
Blood	844	94.7	132.0	6.33				
Heart	797	34.5	35.3	85.0	1.83	17.5	26.1	6.1
Thigh	786	23.3	32.0	86.6	1.72	17.7	27.3	7.5
Puppy W 15, 184 days old								
Serum	919	115.0	147.3	3.98	5.34	2.21	8.60	
Blood	802	88.6	131.0	6.23				
Heart	796	32.0	33.0	75.8	1.71	16.0	29.2	4.5
Thigh	782	19.0	25.8	98.4	1.58	17.6	32.3	7.3
Puppy W 16, 218 days old								
Serum	925	99.2	137.0	3.80	5.42	2.06	8.86	
Blood	799	73.8	119.0	4.60				
Heart	780	28.4	32.7	80.5	1.27	18.2	29.6	5.7
Thigh	774	17.5	20.2	95.0	1.46	17.8	34.0	7.3
Means for Group								
Serum	926	111.4	143.9	4.42	5.44	2.19	8.33	
S.D.†	4	6.0	4.1	0.38	0.12	0.06	0.74	
Blood	797	85.5	123.0	5.95				
S.D.	23	6.8	9.0	0.71				
Heart	794	31.4	26.5	94.6	1.61	17.8	27.9	5.2
S.D.	8	3.0	3.6	4.0	0.09	0.4	1.6	0.6
Thigh	784	20.7	26.5	94.6	1.61	17.8	31.1	7.1
S.D.	5	2.0	3.6	4.0	0.11	0.4	2.1	1.0

* Units are expressed per kilogram of blood-free, fat-free tissue.
† S.D. = standard deviation.

calcium, as well as the total nitrogen and collagen nitrogen, are essentially similar in the two age groups. The chloride and sodium concentrations are significantly decreased in the older group (Table 2), chloride decreasing from 36.7 to 31.4 mEq/kg. and sodium from 34.1 to 26.5 mEq/kg. In the skeletal muscle the findings are similar to those of the myocardium, the only significant changes being a decrease in the chloride content from 29.1 to 20.7 mEq/kg. and in sodium from 34.0 to 26.5 mEq/kg. in the older group.

These findings correspond to those of many other investigators: Iob and Swanson,[16] working on fetus; Hines and Knowlton,[17] on rats; Yannet and Darrow,[18] and Robertson and Peyser,[19] on cats, and Barlow and Manery[20] on chicks.

When the original data are used for the comparison of the two tissues, there is evidence of a superficial similarity between the two types of muscle, cardiac and skeletal, both having decreased amounts of chloride and sodium as age increases. Originally there is less chloride in the thigh muscles than in the cardiac, and this disparity increases in the older age group. There is also a greater amount of collagen nitrogen in the thigh muscles than in the cardiac, indirectly signifying a larger connective tissue content.

Comment

The original data have been submitted to calculations as described in the text in order to obtain histochemical characterizations on the heart and skeletal muscles taken simultaneously from the same animal. Table 3 shows these characterizations. The phase mass data for 1/kg. of blood-free, fat-free tissue are given. First, three examples of each group are given in detail (using the same pups as those for the original data of Tables 1 and 2), and then the means with standard deviations are given for each group intact.

When the assembled data of the young age group (I) are compared with those of the older group (II), many interesting disparities become evident. In considering a kilogram of the heart muscle with aging, there is found a slight increase in the cell mass, $(H_2O)_c + (C)$, from 679 to 714 gm., or a 5% increase, with the maintenance of a striking stable cell water concentration, $\{H_2O\}_c$, of 759 ± 13 and 760 ± 9 gm. This is associated with a decrease of approxi-

TABLE 3.—*Phase Mass Data for Heart and Thigh Muscles* *

M = extracellular compartment + intracellular compartment = (F) + (C).
(F) = grams of extracellular compartment = $(F)_a + (F)_c$.
$(F)_a$ = grams of connective tissue solids in the extracellular compartment.
$(F)_c$ = grams of ultrafiltrate in the extracellular compartment.
$(H_2O)_c$ = grams of intracellular water per kilogram of muscle.
$\{H_2O\}_c$ = grams of water per kilogram of muscle cells.
(C) = grams of intracellular compartment = 1000 − (F), or $(H_2O)_c + (C)_s$.
$(C)_s$ = grams of solids of the intracellular compartment = total solids − $(F)_a$.

	M Gm.	(F) $(F)_a$ + $(F)_c$ Gm.	$(H_2O)_c$ Gm.	$(C)_s$ Gm.	$\{H_2O\}_c$ Gm.
Group I					
Puppy W 11, 87 days old					
Heart	1000	24 + 290	495	182	732
Thigh	1000	45 + 285	518	152	770
Puppy W 12, 120 days old					
Heart	1000	37 + 292	511	160	763
Thigh	1000	56 + 225	563	156	784
Puppy W 20, 119 days old					
Heart	1000	33 + 271	531	165	763
Thigh	1000	44 + 210	586	160	785
Means					
Heart	1000	31 + 290	514	165	759
S.D.†		4 + 9	12	9	13
Thigh	1000	45 + 231	565	150	781
S.D.		6 + 32	29	4	5
Group II					
Puppy W 14, 142 days old					
Heart	1000	39 + 271	526	164	763
Thigh	1000	47 + 183	602	168	783
Puppy W 15, 184 days old					
Heart	1000	29 + 247	549	175	758
Thigh	1000	46 + 147	636	171	787
Puppy W 16, 218 days old					
Heart	1000	36 + 254	526	184	742
Thigh	1000	46 + 156	618	180	774
Means					
Heart	1000	33 + 253	543	171	760
S.D.		4 + 13	13	7	9
Thigh	1000	45 + 167	617	171	782
S.D.		4 + 14	12	7	8

* All values are expressed per kilogram of fat-free, blood-free tissue.
† S.D. = standard deviation.

mately 13%, in the ultrafiltrate volume, $(F)_c$, from 290±9 to 253±13 gm., with the connective tissue solids, $(F)_a$, remaining unchanged. The cell solids increased from 165 to 171 gm. Whether this increase in cell solids is the result of increased enlargement of the heart fibers or an increase in their number cannot be ascertained from this work. Yannet and Darrow [18] have shown histologically that in growth an increase in the size of the individual fibers of the muscle takes place.

In considering a kilogram of the skeletal muscle with aging, there was noted an increase in the cell mass from 724 to 788 gm., or approximately a 9% increase. The cell solids of this phase increased from a mean of 159 to 171 gm. At the same time the ultrafiltrate of the extracellular phase decreased from 231±32 to 167±14 gm., or a decrease of 28%, while the connective tissue solids remained unchanged. The cell water concentration remained constant throughout this growth period—781±5 gm. for Group I and 782±8 gm. for Group II.

When a comparison of heart and skeletal muscle is made, there is found a constant cell water concentration and a constant connective tissue solid weight for the groups of tissue, although there is a greater amount of connective tissue in skeletal muscle and a greater cellular concentration of water in thigh than in myocardium. The initial ultrafiltrate water in skeletal muscle was low as compared with cardiac muscle, and with age the disparity becomes even more marked. A similar decrease in ultrafiltrate water has also been noted in other tissues, such as cartilage,[21] during the aging process.

It is interesting that heart tissue in a growing organism does not change in the mass of its tissue phases as markedly as is found in skeletal muscle. Initially the extracellular phase mass of the heart was larger by 14% than that of skeletal muscle. Furthermore, this extracellular phase mass

of the heart consisted of a 20% larger ultrafiltrate volume and, at the same time, a 5% smaller connective tissue phase. During the period of growth covered in this study the heart extracellular phase mass was decreased only 11%, while the skeletal muscle was decreasing 20%. Simultaneously there was only a 4% increase in the proportion of heart fiber solids, while a 7% increase occurred in the skeletal muscle fiber solids. It should be emphasized that the concentration of water in the heart fibers as well as in the skeletal muscle fibers was constant during this growth period, although the concentration of water in heart fibers was lower in value than that found in skeletal muscle fibers.

From the histochemical patterns of these tissues just presented, which showed that there was a decrease in the mass of the extracellular phase and an increase in the cell solids in each of these tissues during a designated growing period, it was logical to determine whether the composition of the tissue cells and the nature of the extracellular compartment had changed during this period. In the normal organism, potassium and magnesium are confined largely within the cells, and sodium and calcium are largely extracellular. With this in mind, calculations have been made showing the distribution of potassium, magnesium, sodium, and calcium in the muscle phases, and these are presented in Tables 4, 5, 6, and 7, respectively.

After the total content of each constituent was corrected for the amount in the extracellular phase (F), the remaining portion was assigned to the tissue cells (C). From this value, the concentrations were expressed per kilogram of muscle cells and also per kilogram of cell water. From Tables 4 and 5 it is observed that the distributions of potassium and magnesium are the same in the two age groups for each of the tissues. This finding supplements the postulation of Lowry and Hastings[22] "that a given cell regardless of age has a composition restricted within narrow limits." In other words, the growth of cytoplasm must be accompanied by the formation of potassium and magnesium in a concentration that is proportional to the concentration already in the fibers of the tissue. It must be noted, however, that the concentration of potassium in the heart fibers, whether expressed per kilogram of fibers or per kilogram of fiber water, is lower than that found in skeletal muscle fibers, although the magnesium concentrations are approximately the same for the two tissues. Occurring with these lower potassium heart fiber values is a lower con-

TABLE 4.—*Distribution of Potassium Between Serum and Heart and Thigh Muscles* *

$[K]_e$ = milliequivalents of potassium per kilogram of extracellular water.
$(K)_w$ = milliequivalents of potassium per kilogram of muscle.
In $(F)_e\Delta_{Cl}$ = milliequivalents in the ultrafiltrate of the extracellular compartment that is not associated with the connective tissue solids.
$(F)_e\Delta_{Cl}$ = grams of ultrafiltrate in the extracellular phase calculated from ΔCl. The Cl was obtained by calculating first the chloride associated with the connective tissue solids $(F)_e = 20.65 \times (F)_s/100$, and then subtracting this amount from the total muscle chloride, $(Cl)_w$. This difference has been called ΔCl.
Assoc. with $(F)_e$ = milliequivalents of potassium associated with the connective tissue solids in the extracellular compartment = $3.4 \times (F)_s/100$.
In (C) = milliequivalents of potassium in the intracellular compartment = $(K)_w - (F)$.
$\{K\}_c$ = milliequivalents of potassium per kilogram of muscle fibers = $(K)_c/(C) \times 1000$.
$[K]_c$ = milliequivalents of potassium per kilogram of muscle fiber water = $(K)_c/(H_2O)_c \times 1000$.

Tissue	$[K]_e$	$(K)_w$	(F) In $(F)_e\Delta_{Cl}$	(F) + Assoc. with $(F)_e$	In (C)	$\{K\}_c$	$[K]_c$
	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.
Group I							
Heart, Mean	4.81	75.4	1.15	1.04	73.3	108.0	142.2
S.D.†	0.11	3.1	0.08	0.14	3.0	3.9	5.2
Thigh, Mean	4.81	90.2	0.79	1.53	88.0	121.3	155.5
S.D.	0.11	4.5	0.11	0.14	5.0	3.3	4.5
Group II							
Heart, Mean	4.53	78.7	0.92	1.26	76.6	108.2	142.2
S.D.	0.11	4.1	0.10	0.28	4.0	6.3	6.8
Thigh, Mean	4.53	94.5	0.45	1.52	92.6	117.6	150.2
S.D.	0.11	4.0	0.33	0.08	4.0	4.0	4.5

* Units are expressed per kilogram of blood-free, fat-free tissue.
† S.D. = standard deviation.

TABLE 5.—*Distribution of Magnesium Between Serum and Heart and Thigh Muscles* *

Tissue	$[Mg]_s$ mEq.	$(Mg)_w$ mEq.	In (F) mEq.	In (C) mEq.	$[Mg]_c$ mEq.	$\{Mg\}_c$ mEq.
Group I						
Heart						
Mean	1.56	15.9	0.44	15.40	22.7	30.0
S.D.†	0.17	1.1	0.06	1.20	1.6	1.8
Thigh						
Mean	1.56	16.3	0.36	15.90	21.9	28.2
S.D.	0.17	1.3	0.05	0.90	1.5	2.2
Group II						
Heart						
Mean	1.78	17.3	0.47	16.8	23.5	31.0
S.D.	0.05	0.8	0.10	0.9	1.3	1.8
Thigh						
Mean	1.78	17.8	0.30	17.51	22.6	28.4
S.D.	0.05	0.4	0.03	0.18	1.1	0.8

* Units are expressed per kilogram of blood-free, fat-free tissue.
† S.D.=standard deviation.

centration of cell water than that found in skeletal muscle. Since there are many intracellular reactions that are controlled in part by the nature and amount of potassium, this low potassium concentration of the heart fibers could play a role in the prevention of too rapid an increase in the size of the heart fibers as the animal grows older.

The position of sodium, like chloride, is essentially extracellular in both the heart and the skeletal muscle. When the determined values for sodium, $(Na)_D$, are corrected for the amount of sodium in the extracellular phase, (F), we find only a small amount of sodium remaining, which we have labeled ΔNa.

The calcium values were treated in the same way as the sodium values. That is, after the correction of the total calcium content, $(Ca)_M$, of the tissue for the extracellular calcium, there remains an amount that we have labeled ΔCa. Unfortunately, we could not correct for the amount of calcium associated with the connective tissue fibers, for this value has never been determined. The location of the excess sodium and calcium cannot be stated at this time. It is pertinent to know, though, that we would have obtained approximately the same histochemical patterns for these tissues if we had used sodium values to calculate the phases of the tissues, instead of the chloride values.

With the presentation of the histochemical patterns obtained on the heart and skeletal muscle from the normal-growing organism, we were able to estimate the intracellular concentrations of certain constituents of heart and skeletal muscle, notably, water, potassium, and magnesium, and the extracellular composition as well. The constancy of the fiber concentrations of the constituents considered here is of value when abnormal conditions are provoked in an organism. Determining the histochemical characterization of a tissue therefore allows

TABLE 6.—*Distribution of Sodium Between Serum and Heart and Thigh Muscles*

Tissue	$[Na]_s$ mEq.	$(Na)_w$ mEq.	(F)		ΔNa * mEq.
			$(F)_c \Delta_{ci}$ + Assoc. with $(F)_s$ mEq.		
Group I					
Heart					
Mean	149.9	41.2	37.5	6.3	2.5
S.D.	1.2	1.3	3.2	0.9	1.2
Thigh					
Mean	149.9	34.0	23.9	9.0	3.1
S.D.	1.2	2.2	4.2	1.2	0.9
Group II					
Heart					
Mean	147.3	35.4	29.7	6.7	2.3
S.D.	4.5	1.3	2.0	0.7	1.4
Thigh					
Mean	147.3	26.5	14.4	9.1	3.2
S.D.	4.5	3.6	2.8	0.9	1.8

* ΔNa=difference between determined sodium and estimated sodium in (F).

TABLE 7.—*Distribution of Calcium Between Serum and Heart and Thigh Muscles*

Tissue	$[Ca]_s$ mEq.	$(Ca)_m$ mEq.	In (F) mEq.	ΔCa * mEq.
Group I				
Heart				
Mean	2.99	1.93	0.86	1.07
S.D.	0.12	0.12	0.03	0.12
Thigh				
Mean	2.99	1.93	0.68	1.25
S.D.	0.12	0.14	0.07	0.09
Group II				
Heart				
Mean	3.00	1.94	0.76	1.18
S.D.	0.11	0.66	0.05	0.70
Thigh				
Mean	3.00	1.61	0.51	1.11
S.D.	0.11	0.09	0.06	0.09

* ΔCa = difference between determined calcium, $(Ca)_m$, and estimated calcium in (F).

the investigator not only to ascertain changes in the proportion of tissue cells to the extracellular fluid and connective tissue solids, but also to distinguish real changes in the composition of the tissue cells.

Summary

Histochemical patterns for the heart and skeletal muscle removed simultaneously from two groups of puppies, ranging from 87 to 218 days of age, are presented. To summarize the histochemical changes during this growth period, the following deductions were made on both tissues:

1. There was a decrease in the mass of extracellular phase represented entirely by a decrease in the ultrafiltrate, as the connective tissue solids in this phase remained the same for each tissue throughout this allotted span of life.

2. There was an increase in the cell solids—nearly twice as much in the skeletal muscle as in the heart.

As a consequence of these patterns, the concentrations of water, potassium, and magnesium in the fibers of both tissues were calculated after deducting their extracellular quanta. No alterations were found in the concentrations of these constituents in the fibers (intracellular phase) during this growth period. The concentrations of water and potassium in the heart fibers were lower than those found in the skeletal muscle fibers.

It is of considerable significance undoubtedly that the heart tissue did not change in the mass of its tissue phases as distinctly as did the skeletal muscle during the same allotted time of growth. While the skeletal muscle extracellular fluid phase was decreasing by 28% of its weight, the heart extracellular fluid mass was decreasing by only 3%. Simultaneously, the fiber solids weight of the skeletal muscle increased 7%, while the heart fiber solids were increasing 4%.

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Respiratory Arrest Following Intraperitoneal Administration of Neomycin

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As the uses for antibiotics in medicine and surgery have become more widespread and frequent, and as the number of available antibiotic agents has increased, an ever-growing list of complications to these drugs has been reported. These range from the commoner and less serious reactions, such as urticaria, drug fevers, and rashes, to the potentially fatal complications, such as superinfections and acute pseudomembranous enterocolitis. While most of these untoward effects have been frequently reported and are well documented, there are certain rarer, less well-known complications of antibiotic therapy. It is the purpose of this report to present a case of one such complication—respiratory arrest following the intraperitoneal administration of neomycin—and thus to emphasize the potential danger of the administration of the drug by this route. This complication has received only slight attention in the literature, and it is believed that the present case is the sixth to be reported.

Report of a Case

The patient, a 65-year-old white woman, on April 25, 1956, underwent an exploratory laparotomy for acute colonic obstruction. An obstructing neoplasm of the sigmoid was identified and a transverse loop colostomy performed. An uneventful recovery ensued, and on May 11 the patient underwent a sigmoid resection. This included ligation of the inferior mesenteric artery flush with the aorta and a wide resection of the sigmoid mesentery. Her postoperative course was satisfactory; however, barium enemas and sigmoidoscopy done prior to proposed closure of the colostomy revealed an apparent anastomotic stricture. Accordingly, on Oct. 12 another laparotomy was performed for repair of the stricture. A moderate number of adhesions were encountered about the anastomosis, and a zone of narrowing was noted at this level. The colon was opened longitudinally across the previous suture line. The bowel lumen was explored with a finger, and in the region of the splenic flexure stool was encountered. It was felt that this had come across the loop of the colostomy. When the finger was withdrawn, fecal contamination of the peritoneal cavity occurred. The colotomy was then closed in layers in a transverse manner, thus correcting the stricture. Because of the fecal contamination, it was decided to instill neomycin solution into the peritoneal cavity. The proposed dose was to be 50 ml. of a 1% solution. By error the drug was mixed as a 10% solution. This was not known to the operator, and therefore 5 gm. of neomycin sulfate was introduced into the open abdomen. Within 10 minutes the anesthetist announced that the patient was not breathing. She had been receiving a combination of cyclopropane, ether, and oxygen by face mask. An endotracheal tube was passed immediately, but respiratory exchange appeared to be inadequate. A tracheostomy was therefore performed, and the endotracheal tube passed through the stoma. After this, adequate oxygenation of the patient could be maintained by pressure on the breathing bag. Attempts were then made to stimulate respiration by having the patient breathe CO_2 and by injection of lobeline. These methods were unsuccessful. A respirator was then ordered from another hospital, and the patient was maintained on artificial respiration by means of the anesthesia machine. At no time during the entire episode was there any evidence of cardiac arrest or any abnormality of cardiac rhythm. The respiratory arrest occurred at 10:45 a.m. At 5:00 p.m. the patient was placed in a respirator. At 7:00 p.m. she was able to respond to verbal commands, but was unable to breathe on her own. At 1:30 a.m. on Oct. 13 she was able to maintain respiration with the respirator turned off. She had therefore been through 15 hours of respiratory arrest. The tracheostomy tube was removed the following day. Her further postoperative course was uneventful.

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Comment

A review of the American literature has revealed reports of five similar cases. Four of these were collected and reported by Pridgen.[1] Two of the patients were infants, and both died. The other two were adults, both of whom received 3 gm. of neomycin intraperitonealy. Both these patients survived, one after 3 hours, and the other after nearly 48 hours, of respiratory arrest. The fifth case is recorded in the case report section of the American Society of Anesthesiologists' *Newsletter*.[2] In this case an adult was given 2 gm. of intraperitoneal neomycin sulfate following a laparotomy and developed respiratory arrest within 10 minutes. Respirations returned after six hours of arrest, but the patient did not survive.

Pridgen, in his paper cites Poth as stating that the toxic response to the intraperitoneal administration of neomycin in laboratory animals is respiratory arrest, and that these animals may be maintained for many hours by artificial respiration. No other similar statement regarding the potential danger of this route of administration of the drug has been found in the literature, although the nephrotoxic and ototoxic complications of neomycin have been stressed, and are well known. It therefore seems apparent from the present case, as well as from the other cases which have been reported, that intraperitoneal neomycin therapy carries considerable risk, and that with regard to dosage the margin of safety is low. Poth[3] has stated that a total of 4 gm. of a 1% solution may be given during the course of an operation. The tolerance may be somewhat lower if the patient has received preoperative bowel preparation with neomycin. Of the cases under consideration, however, the dose in the one fatal adult case was 2 gm.; in Pridgen's adult cases, 3 gm., and in the case being reported, 5 gm. While it is true that the present patient received an excessive dose in a relatively concentrated solution through an error in the mixing of the neomycin powder, this fact should not minimize the danger of this method of administration.

It is of interest that Schatten[4] recently has reported on the treatment of acute bacterial peritonitis by the intraperitoneal administration of antibiotics. He states that "neomycin is not a toxic drug when it is administered intraperitonealy for 72 hours in large doses." Review of his cases reveals that the drug was given in doses of 1 gm. at surgery, followed by 500 mg. every six hours through an indwelling polyethylene catheter. Thus, while the impression is created that neomycin in large doses may be given by the peritoneal route without fear of toxic effects, it is apparent that Schatten has actually used the drug in a much smaller dosage range than that which has been advocated by others, and than that which has caused respiratory arrest. On the basis of the cases of respiratory arrest which has followed the intraperitoneal administration of neomycin, it would appear that this method for the treatment of peritonitis is potentially unsafe. It should be further stated, however, that all the cases of respiratory arrest occurred in patients who were anesthetized at the time the drug was so given. It is perhaps possible that the toxic action of neomycin is potentiated during anesthesia, or that the effect on respiration may be due to the combined action of several agents.

It should also be noted that there have been no reports of respiratory difficulty following either the oral administration of neomycin or the intraluminal administration of neomycin solution at the time of surgery on unprepared bowel. Whether this merely represents a measure of differential absorption rates, or whether absorption through the intestinal mucosa modifies the toxic potential of the drug, is questionable.

Summary

A case of respiratory arrest following the intraperitoneal administration of 5 gm. of

neomycin sulfate in solution is presented. The patient recovered without sequelae after 15 hours of artificial respiration.

This complication has received slight attention in the medical literature. Only five similar cases have previously been reported.

All cases of respiratory arrest following the intraperitoneal administration of neomycin have occurred in patients who were anesthetized.

When administered by the peritoneal route, neomycin has a low margin of safety, even when given in doses which have been reported to be within safe limits.

The oral and intraluminal routes of administration of this drug appear to have no untoward effect on respiration.

339 Thayer St. (6).

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Intestinal Obstructions

An Analysis of Two Hundred Seventy-Seven Cases with Operation

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Wangensteen [3] pointed out that the judicious use of tube decompression in certain cases of intestinal obstruction, and in the preparation of others for surgery, is an important factor in the management of this condition. Becker [1] has shown how the abuse and misuse of such therapy can lead to disastrous results. Our desire to find out our results in the surgical cases led us into this study.

Material

A total of 277 cases in which operation was performed at our surgical department from Jan. 1, 1947, to Dec. 31, 1955, were reviewed. Most of these patients lived in the San Juan metropolitan area. Included in this study are all types of intestinal obstruction in which operation was done with or without preoperative decompression and the diagnosis was proved either at operation or at autopsy. Cases which were treated by decompression alone are excluded, as their number in the years comprising this study was inaccurately recorded, and we are unable to give a true picture of the results. Also excluded were incarcerated hernias containing omentum only, partial colonic obstructions without proximal dilatation, postoperative ileus, and most cases of adynamic ileus.

Analysis of Data

Etiology.—The cases were classified (Table 3) according to the primary causative agent in the manner described by Wangensteen.[3] The commonest cause of intestinal obstruction was found to be external hernia, which accounted for about one-half the total cases studied. In only 15.9% of the cases was the obstruction due to bands and adhesions. Other important causes were intussusception, neoplastic and inflammatory strictures, volvulus, and imperforate anus, in that order.

Distribution.—There were 174 (62.8%) male and 103 (37.2%) female patients. This difference may be related to the incidence of external hernias, which are more frequent in the male population. Of the 277 patients, 198 (71.5%) white and 79 (28.5%) colored patients were treated. The youngest patient was 2 days old and the oldest 102 years. Thirty patients were less than one year of age (Table 8), but the peak age incidence occurred at 41 to 60 years.

Clinical Picture.—(*a*) Symptoms: From the records it was not always possible to obtain the cardinal symptoms of obstruction in some patients. A history of crampy, colicky, or intermittent abdominal pain was found in 56.7%; 71.5% had vomited; 25.5% complained of distention, and 18%, of obstipation. There were patients who had all four symptoms, while others had only one. Some patients with low obstructions had not noted progressive distention but were found to have been unable to pass feces or flatus for three or more days. Finally, in some cases an adequate history had not been recorded.

(*b*) Physical Findings: Of the patients treated, 70% were found to have been essentially normal. The remainder appeared acutely ill and dehydrated and presented changes in temperature, pulse, and respiration. The commonest abdominal finding was an external hernia, which occurred in 130

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cases (46.9%). The other findings noted, in order of frequency, were as follows: abnormal peristalsis, 43.3% (increased 30.3%, decreased or absent, 13%); tenderness, 39.7%; distention, 37.9%; tympanites, 16.6%, and abdominal mass, 16.2%. Rectal and pelvic examinations were helpful in 21.5% of the cases.

(*c*) Laboratory Data: Since in 84.8% of the cases operation was performed soon after admission, the laboratory tests done were usually limited to complete blood counts, urinalysis, and serology, although more thorough biochemical evaluations have been done lately. These laboratory data were judged of value in only 23.8% of the cases, particularly in determining the status of hydration, anemias, and strangulating obstructions.

(*d*) Roentgen Examinations: These examinations consisted of plain films of the abdomen and barium enema studies. X-ray films were not taken in 127 cases of external hernia and in 53 cases of various other types of intestinal obstruction. In 96 cases roentgen examinations were done, and these were diagnostic in 92.8% of the cases.

Treatment.—Ninety-six patients (34.7%) were admitted with vomiting or distention or both and had intestinal intubation and decompression started with a suction-siphon apparatus. In only very few cases was an attempt made to pass a tube beyond the pylorus. Patients with inflammatory strictures of the rectum sometimes had successful decompressions with finger dilatations and enemas. Attempts to decompress and reduce a case of volvulus of the sigmoid with a proctoscope and a rectal tube were only partially successful. Patients who were vomiting and dehydrated were immediately started on replacement intravenous fluid therapy. In a review of the mode of therapy, the cases could be divided into two groups: those in which operation was performed soon after admission, and those in which there was a delay (Table 10). Included in the first group were infants with obstructions due to congenital anomalies; and patients with the following forms: incarcerated or strangulated hernias, suspected strangulating obstructions, intussusceptions, volvulus, and complete small-bowel or colonic obstructions showing no dehydration. In the delayed group were patients who received decompression usually over 24 hours and included partial intestinal obstructions which did not respond to it, or became complete, or developed signs of strangulation. Delay was also the rule in cases of obstructions at the rectum which were decompressed with dilatations and enemas and, finally, cases in which special diagnostic studies were indicated. Surgical procedures (Table 1) consisted of release of obstruction (67.5%), enterostomy or colostomy (7.9%), operative intestinal decompression (1.1%), and intestinal resection (22%). In four cases only an exploratory laparotomy was performed. Postoperatively, 125 patients (45.1%) who either had bowel resection or presented intestinal distention at operation received nasogastric tube decompression. Most patients were kept on a regimen of nothing by mouth until they had active peristalsis and had passed flatus or feces per rectum or colostomy, receiving replacement intravenous fluid therapy, blood, and antibiotics as indicated. Ambulation was started on the first or second postoperative day, except in extremely debilitated patients.

Complications.—The commonest postoperative complication was wound abscess and hematoma, which occurred in 14 cases (Table 2), of which 7 were in the resection group. The other complications, in order

TABLE 1.—*Operative Procedures in 277 Surgical Cases of Intestinal Obstruction*

Type of Procedure	No. Cases		Percentage	
Release of obstruction	187		67.5	
Enterostomy or colostomy	22		8.0	
Operative intestinal decompression	3		1.1	
Primary intestinal resection	58		20.9	
End-to-end anastomosis		45		16.2
End-to-side anastomosis		2		0.7
Side-to-side anastomosis		5		1.8
Perineal colostomy		6		2.2
Two-stage resection	3		1.1	
Exploratory laparotomy only	4		1.4	
Totals	277		100	

TABLE 2.—*Complications in 277 Surgical Cases of Intestinal Obstruction*

Type of Complication	No. Cases	Incidence, %
Wound abscess and hematoma	14	5.1
Pneumonia and atelectasis	8	2.9
Postoperative distention	8	2.9
Thrombophlebitis	5	1.8
Stricture	5	1.8
Evisceration	4	1.4
Peritonitis	4	1.4
Shock	2	0.7
Cardiac Failure	2	0.7
Miscellaneous	8	2.9
Totals	60	21.6

of frequency, were bronchopneumonia and atelectasis, distention, thrombophlebitis, strictures, evisceration, peritonitis, shock, cardiac failure, and various other miscellaneous ones. There was a total of 60 postoperative complications, for an incidence of 21.6%, of which 19 were in the resection group.

Mortality.—A total of 26 deaths, for an over-all mortality of 9.4%, was observed. However, seven of these deaths were due to causes unrelated to the management of intestinal obstruction, thus giving a corrected mortality of 6.8%. The relation of death to cause of obstruction has been stressed by Wangensteen, and in Table 3 a breakdown of the deaths according to the cause is presented. Our mortality was particularly high in all types of obstructing congenital anomalies in infants, mesenteric thrombosis, neoplastic strictures, and volvulus. One of two patients with primary

TABLE 3.—*Incidence and Mortality* in 277 Surgical Cases of Intestinal Obstruction*

Primary Cause of Obstruction	Total Cases		Total Deaths	
	No.	%	No.	%
Congenital atresia	2	0.7	2	100
Imperforate anus	7	2.5	1	14
Inflammatory stricture	17	6.1	2	11.8
Neoplastic stricture	17	6.1	5	29.4
Obturation by worms	4	1.5	..	..
Megacolon	3	1.1	1	33.3
Congenital bands	9	3.2	1	11
Inflammatory adhesions	2	0.7	..	..
Postoperative adhesions	33	11.9	..	..
External hernia	130	46.9	3	2.3
Internal hernia	5	1.8	..	..
Volvulus	11	4	3	27.2
Intussusception	28	10.1	2	7
Adynamic ileus	2	.7	1	50
Malrotation	3	1.1	2	66.6
Mesenteric thrombosis	4	1.5	3	75
Totals	277	100	26	9.4

* Seven deaths were due to causes not related to the management of intestinal obstruction.

TABLE 4.—*Causes of Death in 277 Surgical Cases of Intestinal Obstruction*

Cause of Death	Small Bowel	Large Bowel	Total No.	Deaths, %
Postop. peritonitis	3	3	6	23.1
Carcinomatosis *	1	4	5	19.2
Postoperative shock	2	1	3	11.5
Mesenteric thrombosis	3	..	3	11.5
Pneumonia and atelectosis	2	..	2	7.7
Coronary thrombosis *	1	1	2	7.7
Electrolyte imbalance	1	..	1	3.8
Unrecognized gangrene	1	..	1	3.8
Pulmonary embolus	..	1	1	3.8
Cardiac arrest	1	..	1	3.8
Cardiac failure	1	..	1	3.8

* Not related to the management of obstruction.

adynamic ileus died after operative intestinal decompression.

Results

The factors which affect the mortality in intestinal obstructions are of particular value, since the rate still remains high. In a manner similar to that used by Smith,[2] a detailed analysis has been attempted. In Table 4 the causes of death are listed in order of frequency. Six patients died of postoperative peritonitis; of these, two patients underwent a resection of the sigmoid, and one had a sigmoid colostomy. Of the other three, one had operative intestinal decompression for paralytic ileus; another, a posterior gastroenterostomy for duodenal atresia, and the third, an exploratory laparotomy and lysis of adhesions for duodenal obstruction due to malrotation of the colon. Three died with extensive mesenteric thrombosis, and one, in frank electrolyte imbalance. Five others died of carcinomatosis and two of coronary thrombosis, their deaths being unrelated to the management of their obstructions. There were three postoperative deaths due to shock and one due

TABLE 5.—*Mortality as Related to Type of Obstruction in 277 Surgical Cases (1947-1955) of Intestinal Obstruction*

Type of Obstruction	No. Cases	No. Deaths	Mortality Rate, %
Simple			
Nonperforated	122	17	13.9
Perforated	4	..	..
Strangulating			
Nongangrenous	113	2	1.8
Gangrenous	38	7	18.4
Totals	277	26	9.4

TABLE 6.—*Mortality as Related to Site of Obstruction in 277 Surgical Cases (1947-1955) of Intestinal Obstruction*

Type of Obstruction	Small Bowel			Large Bowel		
	No. Cases	Deaths		No. Cases	Deaths	
		No.	%		No.	%
Nongangrenous	182	11	6	53	8	15.1
Gangrenous	35	5	15.2	5	2	40
Perforation	2	--	--	2	--	--
Totals	217	16	7.4	60	10	16.7

TABLE 8.—*Mortality as Related to Age in 277 Surgical Cases (1947-1955) of Intestinal Obstruction*

Age, Yr.	No. Cases	No. Deaths	Mortality Rate, %
0-1	30	10	33.3
1-20	49	2	4.1
21-40	63	4	6.4
41-60	71	3	4.2
61-80	56	6	10.7
81-102	8	1	12.5
Totals	277	26	9.4

to cardiac arrest at surgical exploration. In one case of external hernia, early gangrene in a loop of ileum went unrecognized, and the patient died as a result of its perforation. Four patients died of various other postoperative complications.

Type of Obstruction.—There were 126 cases of simple obstruction with 17 deaths, for a mortality rate of 13.5% (Table 5). Four of these had perforations prior to surgery, and none died. In the strangulating, nongangrenous group, which was composed totally of external hernias operated on rather promptly after admission, two patients died, a mortality rate of 1.8%. In the gangrenous group, 7 of 38 patients died, a mortality of 18.4%. Four in this group had a massive intestinal infarction; of these, three died and one was saved by intestinal resection.

Site of Obstruction.—When the small bowel was obstructed (217 cases) there were 16 deaths, a mortality rate of 7.4% (Table 6). Of the 60 patients with large-bowel obstruction, 10 died, a mortality rate of 16.7%. As can be expected, the mortality was over twice as high in the gangrenous type of obstruction, and this was particularly true when it occurred in the large bowel.

Distention.—The cases were divided between those presenting severe distention clinically or by x-ray examination and those with moderate to slight or no distention. In the first group there were 39 cases, and in the second, 238 (Table 7). Mortality was over four times as high (28.2%) in those patients with marked distention when taken to surgery as in those with moderate to no distention (6.3%). Marked distention in cases with gangrene of the bowel was 50% fatal.

Age.—As intestinal obstruction occurs so frequently during the first year of life, the one-year infants were placed in a separate group (Table 8), and the remaining patients were grouped in 20-year periods. One-third of the infants with intestinal obstructions during their first year of life died. Of the rest of the patients, death supervened most frequently in the aged group.

Preoperative Decompression.—In 96 cases intestinal decompression was instituted because of severe vomiting, or severe or moderate distention, or both. Most of these patients were in poor general condition on admission to the hospital. The remaining

TABLE 7.—*Mortality as Related to the Degree of Distention in 277 Surgical Cases (1947-1955) of Intestinal Obstruction*

Type of Obstruction	Marked Distention			Mod. to No Distention		
	No. Cases	Deaths		No. Cases	Deaths	
		No.	%		No.	%
Nongangrenous	29	6	20.7	206	13	6.3
Gangrenous	10	5	50	28	2	7.1
Perforation	--	--	--	4	--	--
Totals	39	11	28.2	238	15	6.3

TABLE 9.—*Mortality as Related to Preoperative Decompression in 277 Surgical Cases (1947-1955) of Intestinal Obstruction*

Type of Obstruction	Decompression			No Decompression		
	No. Cases	Deaths		No. Cases	Deaths	
		No.	%		No.	%
Nongangrenous	72	11	15.3	163	8	4.9
Gangrenous	20	4	20	18	3	16.7
Perforation	4	--	--	--	--	--
Totals	96	15	15.6	181	11	6.1

TABLE 10.—*Mortality as Related to Prompt vs. Delayed Operation 277 Cases (1947-1955) of Intestinal Obstruction*

Type of Obstruction	Prompt			Delayed		
	No. Cases	Deaths		No. Cases	Deaths	
		No.	%		No.	%
Nongangrenous	199	13	6.5	36	6	16.7
Gangrenous	33	6	18.2	5	1	20
Perforation	3	..	..	1	..	..
Totals	235	19	8.1	42	7	16.7

TABLE 11.—*Mortality as Related to Resection in 277 Surgical Cases (1947-1955) of Intestinal Obstruction*

Type of Obstruction	Resection			Others		
	No. Cases	Deaths		No. Cases	Deaths	
		No.	%		No.	%
Nongangrenous	24	2	8.3	211	17	8.1
Gangrenous	35	4	11.4	3	3	100
Perforation	2	..	..	2	..	..
Totals	61	6	9.8	216	20	9.3

patients received no decompression, since this group was composed mainly of those with external hernias who came to the hospital early after onset of symptoms and were operated on promptly after admission. The first group had a 15.6% mortality and the second 6.1% (Table 9).

Prompt Vs. *Delayed Operation.*—Only 42 patients were operated upon 24 hours after admission, and 7 died, a mortality rate of 16.7% (Table 10), whereas for those receiving prompt surgical intervention there was only 8.1% mortality. In cases of nongangrenous obstruction the mortality was higher in the delayed treatment group.

Resection.—There was no appreciable difference in mortality between the resection and the nonresection group (Table 11). However, failure to resect gangrenous bowel was 100% fatal. This occurred in two cases of extensive mesenteric thrombosis and in one case of unrecognized early small-bowel gangrene. In 35 cases of gangrenous obstruction in which resection was performed, 4 patients died, a mortality rate of 11.4%.

Anesthesia.—The breakdown of the anesthetic agents and techniques employed is shown in Table 12.

Comment

It is of interest to note that in Puerto Rico, where repair of external hernias was being done mostly in adults, the incidence of intestinal obstructions caused by them was the highest (46.9%). During the past 10 years an increasing number of children have been undergoing repair of hernias, thus probably affecting the incidence of bowel obstruction from this cause in the future.

The major factors affecting the mortality rate in bowel obstruction continue to depend on the cause, type, and site of obstruction; the degree of distention; the age of the patient; the state of hydration, and the time interval from onset to definitive treatment. In Table 5 one is deceived by the low mortality of the group with nongangrenous strangulating obstruction. However, this group in the present study is made up exclusively of external hernias which were operated on within a few hours after admission. Patients with external hernias came to the hospital usually within a few hours after the onset of symptoms, whereas patients with simple bowel obstruction usually treated themselves at home until distention had developed and their general condition had deteriorated through vomiting, dehydration, and malnutrition. Despite this, the use of preoperative decompression, hydration, and correction of anemia reduced their mortality rate to 13.5%. Had the cases treated by decompression alone been included in this study, the mortality rate represented here would have been even lower.

TABLE 12.—*Anesthesia Used in 277 Surgical Cases (1947-1955) of Intestinal Obstruction*

Type of Anesthesia	No. of Cases
Spinal	151
Ether (drop)	74
Endotracheal	19
Local	17
Pentobarbital Na	16
Totals	277

Summary and Conclusions

An analysis of 277 cases of intestinal obstruction operated upon between Jan. 1, 1947, and Dec. 31, 1955, at San Juan City Hospital has been made.

The over-all mortality rate was 9.7%, and the corrected mortality rate, 6.8%.

The factors influencing the mortality are reviewed.

External hernia is the most frequent cause of bowel obstruction in our hospital, and the results of its treatment carry one of the lowest mortality and morbidity rates in this series.

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In Vitro Oxygenation of Fresh Whole Blood for Arterial Perfusion

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With the elucidation of the "azygos flow factor" by Andreason and Watson,[1] it was established that a markedly reduced venous return and cardiac output were compatible with prolonged survival in dogs. Lillehei[2] has demonstrated that with caval occlusion produced at normal body temperature azygos vein flow into the right atrium is compatible with survival for periods of 30 to 60 minutes. In dogs this flow amounted to 8 to 14 ml. per kilogram of body weight per minute and was less than 10% of the basal cardiac output. The clinical application of this principle resulted in "cross circulation procedures," with blood flow between donor and patient regulated in the range of 20 to 25 ml. per kilogram per minute. This technique permitted open right cardiotomy and the surgical repair of congenital defects of the interatrial and interventricular septa.

Recently, in many laboratories, pump oxygenators have been developed to the point of clinical usefulness. Without exception, their application remains complex and dependent on a highly organized team for successful operation.

Symptoms secondary to congenital defects of the right heart usually are apparent in early childhood in patients with body weights in the range of 5 to 15 kg. Perfusion of the coronary arteries, afferent cerebral vessels, and systemic circuits with preoxygenated blood during caval occlusion could be carried out in these children for 10 minutes, with 2 to 3 liters of blood.

A second application for preoxygenated blood transfusions may be found in cardiac surgery under hypothermia.[3] At the present time the maximum period of circulatory occlusion (vena caval occlusion) is limited to 10 minutes, with myocardial anoxia and irritability greatly increased at the end of this interval. However, if the coronary and cerebral afferent vessels are perfused with oxygenated blood at flow rates of 200 to 300 ml. per minute, occlusion time may be prolonged and ventricular irritability decreased.[4]

Although "once-through" perfusion is wasteful of blood, its use can be justified by the reduction of hazard for the patient through the use of a preoxygenated and bubble-free supply of fresh blood, which can be delivered with the use of routine transfusion equipment.

We have demonstrated that blood can be fully oxygenated in vitro in a closed aseptic system with use of standard plastic equipment with minimum foaming and entrainment of bubbles. The blood can be obtained from donors previously cross matched against the recipient, and collected, oxygenated, and stored prior to use without demonstrable degradation.

Hannon, Alden, and Baronofsky[5] showed that ordinary A. C. D. (acid citrate-dextrose)-banked blood can be oxygenated to a level where it might be useful for cardiac and cerebral perfusion. This method has been reported[6,7] to be in routine use in Poland and Russia in support of abdominal and thoracic surgery and for the treatment of shock. However, the advantages of a

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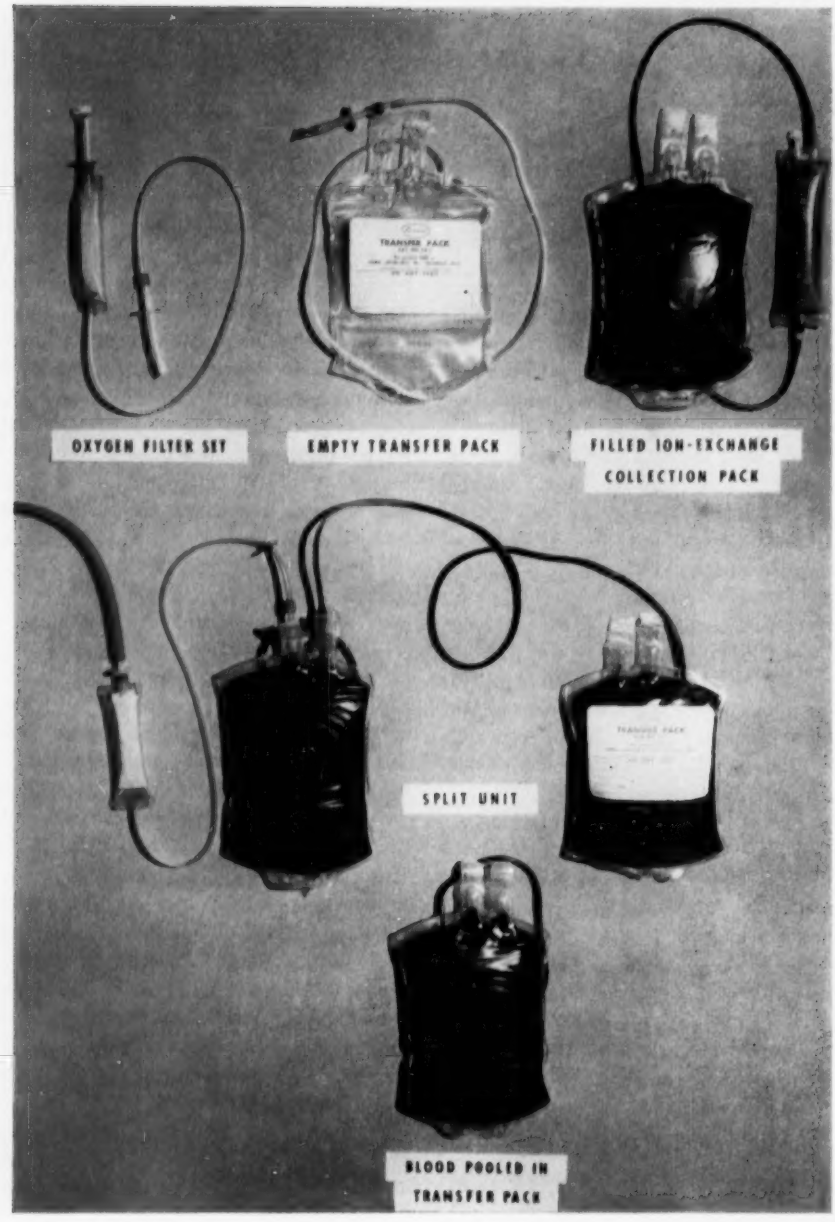

Fig. 1.—Method of oxygenation.

Top row: Equipment required for collection and oxygenation. From left to right: oxygen filter set, transfer pack, and filled ion-exchange collection pack.

Center row: The blood is split between the collection pack and the sterile transfer pack. The oxygen filter set (left) is connected to the original collection pack.

Bottom row: Fully oxygenated blood pooled in transfer pack ready for perfusion.

high percentage of viable red cells, a normal pH, and the absence of citrate or other anticoagulant suggests the use of unadulterated fresh blood. This can be obtained by collection through ion-exchange columns[8] from previously cross matched donors. Although, under normal circumstances, this would be done within 48 hours of the scheduled operation, blood collected by this technique has been shown[9] to have the same red cell survival without addition of a substrate as has blood collected in A. C. D. solution up to 10 days. After this, dextrose and buffer capacity is exhausted, and the viable cells decrease rapidly.

Procedure

Blood is collected from donors through a plastic ion-exchange column into a plastic bag. After collection, the donor tube is tied off and the column separated in the usual fashion.[8] An empty, sterile 600 ml. transfer pack which is identical with the plastic blood pack is plugged into one of the outlet ports of the full blood pack. Approximately one-half of the blood is then allowed to flow into the transfer pack. A special oxygen filter set (Fig. 1) is then plugged into the other port of the transfer pack, and the chamber coupler, into a length of rubber tubing attached to an oxygen bottle reducing valve. The chamber of this set may be filled with sterile saline, if desired, and used to hydrate the oxygen. Oxygen is then allowed to flow into both packs until swelling indicates that uptake is complete. This takes approximately five minutes. The packs are gently agitated to hasten oxygenation, with the connecting tubing upright so that gas can flow into the transfer pack.

Upon completion of this process, the gas is shut off; the gas supply tube is knotted or sealed and then severed. All the blood is allowed to run into the transfer pack, and the residual oxygen is expressed into the original blood pack. The donor tube is then knotted and severed. The blood is stored under refrigeration until used.

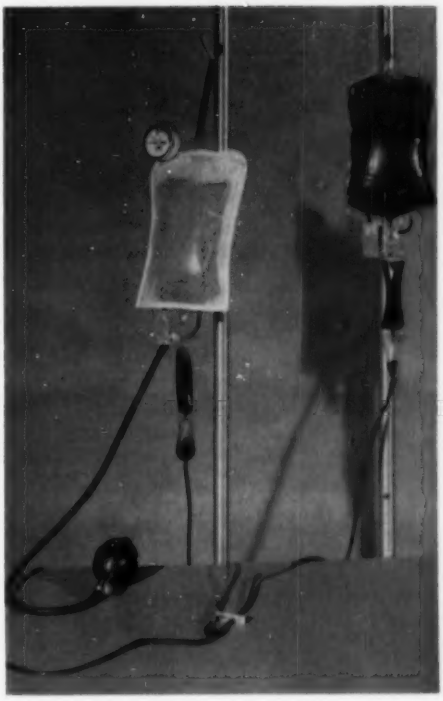

Fig. 2.—Two bloods coupled into a standard anesthesia-type recipient set for continuous infusion. Only one is shown with the pressure infuser for clarity of illustration. In practice, two infusers would be used.

Rapid continuous infusion of the oxygenated blood is obtained with the use of the two pressure infusers, an anesthesia-type recipient set,* and a standard recipient set. Any number of bloods can be continuously and rapidly infused with no cessation of flow, using this equipment. Flow rates up to 300 ml. per minute can be obtained.

Initially, two bloods are set up, with one plugged into the anesthesia set and the other plugged into the standard set (Fig. 2). Infusion is started with only one blood running. When this bag is empty, the other is unclamped, and the empty pack is replaced with another, full bag. Owing to the high filtration capacity of the recipient sets, several bloods can be run through a given set without diminution of the flow rate.

* Ethicon, Inc., Somerville, N. J., Cat. #HB-382.

TABLE 1.—*Ion-Exchange Blood: In Vitro Determination Studies*

Exper. No.	Age, Days	O_2 Content, Vol. %	O_2 Content, % Saturation	Osmotic Fragility, % Hemolysis		Plasma K, mEq/L.	Plasma pH	Plasma Hbg, Mg/100 Ml.
				0.85% NaCl	0.6% NaCl			
0-2	0	20.97	103.5	0	0	1.0	7.51	8.0
	1	20.2	104.5	0.8	1.0	7.0	7.60	4.0
0-3	1	16.3	107.0	1.0	2.0	7.0	7.48	8.0

TABLE 2.—*Heparinized Blood: In Vitro Studies*

Exper. No.	Age, Days	O_2 Content, Vol. %	O_2 Content, % Saturation	Osmotic Fragility, % Hemolysis		Plasma K, mEq/L.	Plasma pH	Plasma Hbg, Mg/100Ml.
				0.85% NaCl	0.6% NaCl			
0-1	0	20.12	108.0	0	2.5	1.0	7.51	8.0
0-1	1	20.52	109.0	0	2.5	7.0	7.60	8.0
0-4	1	19.07	109.5	0	0.6	7.0	7.52	10.0

An elaboration of this technique has been reported by Brown et al.[10] wherein special plastic bags are used to collect blood from an extracorporeal circulation pump. The blood is oxygenated in the bag and then returned to the systemic circulation.

The in vitro determinations (Tables 1 and 2) demonstrate the oxygen-storage capacity of blood collected through ion-exchange columns. Oxygen levels were determined† with the Van Slyke apparatus; osmotic fragilities by a modification of Parpart's method,[11] and plasma hemoglobin levels by the benzidine technique.

These experiments demonstrated that blood could be oxygenated and stored for limited periods without a substrate and maintain its oxygen level. The oxygen content in excess of 100% was interpreted to be dissolved oxygen, which would probably combine with the recipient's circulating red cells or be directly available for metabolic requirements.

A further demonstration of the feasibility of this procedure was shown by in vivo survival studies (Table 3). Blood was collected from three normal volunteers and oxygenated by the method described above. After storage, an aliquot of the blood (about 100 ml.) was removed, tagged with Cr^{51}, and its post-transfusion survival determined by the method of Gibson.[12] The results were in agreement with Emerson's[9] findings for unoxygenated ion-exchange blood, and the bloods satisfied the arbitrary requirement that 70% of the red cells survive in the recipient's circulation 48 hours after transfusion.

† Miss Barbara Jacobs performed the oxygenation studies.

Summary

A simple closed system for the in vitro oxygenation of whole blood and a method for perfusion are described.

Maximum oxygenation of red cells was found to be maintained during storage.

Transfusion of Cr^{51}-tagged preoxygenated whole blood into normal volunteers demonstrated normal red cell life.

Mrs. Ruth B. Kundsin assisted in the bacteriologic studies.

Peter Bent Brigham Hospital.

TABLE 3.—*Ion-Exchange Blood: In Vivo Studies*

Exper. No.	Subject		Days Stored	Post-transfusion Survival, %	O_2 Content,* Vol. %	O_2 Content,* % Saturation	Osmotic Fragility, % Hemolysis		Plasma K, mEq/L.	Plasma pH
	Sex	Age					0.85% NaCl	0.6% NaCl		
0-5	F	22	4	87	17.15	107	....	6.2	14	....
0-6	M	24	6	82	19.7	102.3	3.4	10.8	15	7.41
0-8	M	21	8	76	21.65	110	3.2	28	14	7.42

* O_2 studies made on day of transfusion.

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The Persimmon Bezoar

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DeBakey and Ochsner [1] have stated that the subject of bezoars forms an intensely fascinating and interesting study, not only because of their relatively infrequent occurrence and bizarre nature but also because of the mystical lore surrounding their early development. The truth of this statement is apparent when one investigates this subject. This paper is prompted by the discovery of a persimmon bezoar in the stomach of a patient who had consumed wild persimmons while on a recent hunting expedition along the Illinois River. Isolated reviews through the years indicate the rarity of the lesion, at least in this part of the country, hence the presentation of the features of a case which came to surgery shortly after the ingestion of the fruit.

Among the early reports on this condition is that of Hart,[2] who in 1923 reviewed eight surgically treated cases of phytobezoars, six of which were recorded as of the persimmon variety. The most complete and exhaustive report on the subject of bezoars of all kinds is that of DeBakey and Ochsner, who collected 311 cases. For the 126 collected cases of phytobezoars, these authors suggested the term "diospyrobezoar," from the Greek etymon "diospyron," meaning Jo's grain, from which comes the generic name for the wild persimmon. In a paper covering the period from 1894 to 1934, Durrance [3] compiled 35 reports of known phytobezoars of persimmon origin. Two varieties of the native persimmon are described, namely, the eastern (Diospyros virginiana), which is common to the southern and eastern United States, and the Mexican (Diospyros texana), common in Texas and Mexico; but there were no reported cases due to the Japanese persimmon (Diospyros kaki), which is cultivated extensively in the southern states. In 1950, Tondreau and Kirklin [4] reported 13 cases of proved persimmon bezoars removed at the Mayo Clinic. In 1953 O'Leary,[5] of the University Hospital at Oklahoma City, reported six additional cases of these diospyrobezoars with a definite history of the ingestion of persimmons and presented an analysis of 46 cases collected from the literature.

White [6] stated that persimmon bezoars are more frequent than all the other food bezoars combined. The persimmon-seed bezoars are derived from the ingestion of the wild-plum-like fruit, which is orange-colored, has a sweet taste, and contains multiple seeds. The ingestion of this readily available fruit is quite prevalent among men on hunting or fishing trips and farmers in the field, and has even been reported among golf enthusiasts. It is surprising that not more of these bezoars are encountered.

There are various theories as to the mode of formation of these bezoars. Pollok [7] and other authors have stated that fresh, ripe persimmons contain a high percentage of gum and pectin, suggesting that this must be a significant factor. When they are eaten raw and combined with fibrous food, cohesion is favored by muscular activity, and a mold of indigestible material may remain in the stomach. However, it is still not well known why the condition should occur in some persons, whereas others remain entirely free after eating the same food. The experimental work of Chont,[18] reported in 1942, suggested that the incompletely ripe

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persimmon forms bezoars in any solution of hydrochloric acid, with or without pepsin, but not in water or alkaline solutions. Izumi and his associates [8] have offered an explanation for the production of these intragastric masses. In vitro experiments indicated that gastric juice is capable of precipitating a soluble substance, called shibuol, a phlobatannin, present in large amounts in the unripe persimmon; however, even in the ripe fruit traces of soluble shibuol may be found. The process of ripening produces coagulation of shibuol. This suggests that with an empty stomach the eating of unripened or unpeeled ripened persimmons permits coagulation of the so-called phlobatannin. A bezoar is then formed by the aggregation of fragments of seed and skin. There is a suspicion that the formation of these persimmon bezoars is immediate, especially when the stomach is devoid of food, and results from the eating of a large quantity of fruit at one time.

These foreign bodies within the stomach are found more commonly in males. They are putty-like, compact masses, which vary in size and are frequently multiple, and may form a palpable mass in the upper abdomen. They have an irregular, greenish-black surface and a yellow-pink interior, containing undigested fruit and seeds. These solid masses manifest themselves clinically by the degree of gastrointestinal discomfort they produce. The symptoms vary in character and intensity. Acute abdominal symptoms, appearing within 24 hours after the ingestion of the fruit, may become less profound over a period of time. Nausea and vomiting are variable. In some cases, extreme symptoms have developed of anorexia, loss of weight, and alternating diarrhea and constipation, suggesting a picture which closely resembles malignancy. However, there are other cases reported of long standing in which the patient is in surprisingly good condition with little evidence of loss of weight. Although severe hematemesis associated with persimmon bezoars has been rarely described, Smith [9] reported two such cases in which massive gastric hemorrhage occurred. In one case a large stomach ulcer had perforated into the pancreas, simulating an advanced carcinoma. White [6] has emphasized that hemorrhage associated with a bezoar, diagnosed roentgenologically as an inoperable malignancy of the stomach, should require exploration to rule out any doubts. Numerous cases are reported in which a gastric ulcer, presumably traumatic, is found in the presence of the bezoar. This finding was present in a high incidence of O'Leary's cases (71%). Colic-like pain of intestinal obstruction may result when the foreign body has slipped into the intestine. Accordingly, hemorrhage, ulceration, gastrointestinal obstruction, and perforation with peritonitis characterize the more serious complications of these bezoars.

The diagnosis of a persimmon phytobezoar is established by fluoroscopic examination of the stomach, and, as an additional aid, Moersch and Walters [10] have advocated direct visualization by means of the gastroscope. The appearance of most bezoars is striking with the aid of a barium examination. Actually, the filling defect of the persimmon bezoar may be observed above the level of the barium meal. Too much barium given initially may obliterate a small bezoar or cause one to overlook a second, similar mass. Hart [2] reported such a case treated by A. F. Sippy and C. B. Davis. The gastric analysis of acidity (hydrochloric acid), as well as blood studies, varies considerably in these cases.

The treatment of a persimmon bezoar of the gastrointestinal tract consists of early surgical removal; however, Eusterman and Balfour [11] cite examples of simpler methods of therapy than surgery. Outten is said to have quoted King's account of a case in which massage of the stomach was instituted while the patient was awaiting surgery. After two weeks, the palpable tumor disappeared with the passing of seeds. This treatment is obviously inconclusive, as well as hazardous, in patients with a gastric ulcer. Catharsis has been reported as resulting in

the disappearance of an epigastric mass and passage of seeds in one patient who gave a history of eating persimmons. Actually, some years ago, Vinson and Deissler stressed the importance of a period of observation and medical treatment before advising surgical removal of foreign bodies in the stomach.

The first recorded incident of successful surgical removal of a gastric persimmon bezoar was reported by Outten in 1894.[12] Rodgers, in 1937,[13] reported the removal of two black foreign bodies of persimmon origin. Removal of a gastric bezoar is readily accomplished through a transverse incision made in the anterior wall of the stomach midway between the lesser and the greater curvatures. During the removal of a foreign body from the stomach, fragmentation must be avoided since concretions may be residual. Examination of the stomach for ulcer is recommended as penetration or perforation of an ulcer has resulted in death in reported cases; however, a number of authors maintain that an associated gastric ulcer will heal spontaneously following removal of the bezoar. Balfour and Good[14] reported a case with roentgenograms, demonstrating an ulcer on the lesser curvature and a filling defect high in the stomach, which was considered to be a benign tumor. A partial gastric resection included the ulcer and the intragastric mass which proved to be a persimmon bezoar. On further questioning, the ingestion of persimmons was recalled by the patient while out hunting earlier. Surgical exploration should not be denied patients who present signs and symptoms of gastric malignancy, as the persimmon bezoar may simulate cancer. David[15] reported the case of a 59-year-old woman whose preoperative diagnosis was a penetrating gastric ulcer of the lesser curvature, "most probably malignant." At operation, in addition to the ulcer, there was found a totally unsuspected foreign body which after removal was found to be a persimmon bezoar.

McCarley and Greenberger[16] reported a somewhat similar case of a persimmon phytobezoar which was incorrectly diagnosed roentgenologically as carcinoma of the stomach. Two months later, another fluoroscopic examination revealed the true findings in the stomach: a phytobezoar associated with a large penetrating ulcer on the lesser curvature of the stomach. These findings were substantiated at operation.

The operative mortality in recent years is obviously low as compared with Maes' reference[17] to Matas' early paper of 1912, in which the operative mortality in 47 cases of all kinds of bezoars was 4%.

Report of a Case

The patient, aged 49, was admitted to the Presbyterian-St. Luke's Hospital of Chicago on Nov. 20, 1956. The patient stated that he had experienced a dull, aching abdominal pain associated with nausea and vomiting shortly after returning from a quail-hunting trip. On the afternoon of that day he ingested a large number of wild persimmons. That evening he noted a very full feeling in the epigastrium. At 3 o'clock the next morning he was awakened by a sharp, burning epigastric pain and a feeling of nausea. He was able to vomit a dark-brown material free of food particles. For the next 24 hours his intake included only water, milk, and crackers. Some alkali relieved the epigastric distress. No blood was observed in the stool.

The past history revealed that the patient had experienced numerous attacks of pain in the epigastrium and a feeling of fullness which radiated into the left chest, particularly the precordium. Repeat electrocardiograms in the past had shown no evidence of coronary occlusion. A stomach fluoroscopy two weeks prior to admission was negative for a gastric or duodenal ulcer. Stool examinations were negative for blood at that time.

Admission to the hospital was approximately 48 hours after the onset of symptoms. The patient stated that he was weak. He complained of vague upper abdominal distress associated with marked anorexia. The temperature, pulse, and respirations were normal. The blood pressure was 140/70. Heart examination showed a regular rate and rhythm. No murmurs were heard. The lungs were clear. No abdominal distention was noted, and there was no palpable mass in the epigastrium.

The laboratory work-up was reported as follows: hemoglobin, 14 gm. per 100 cc.; red blood cell count, 4,620,000, and white blood cell count, 10,800, per cubic millimeter. The urine was negative. An

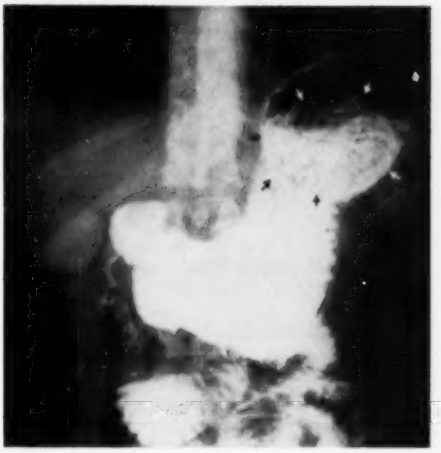

Fig. 1.—Roentgenogram of the stomach demonstrating the persimmon bezoar "floating" above the barium.

electrocardiogram was within normal limits. The patient was treated symptomatically. The clinical impression was acute gastritis with the possibility of coronary thrombosis. Two days after admission, a fluoroscopic examination of the stomach revealed a movable, irregularly shaped intragastric mass characteristic of a foreign body (Fig. 1). With the history of the recent ingestion of persimmons, the preoperative diagnosis was a persimmon bezoar. Surgical exploration was recommended.

On Nov. 28, the peritoneal cavity was opened through an upper abdominal midline incision. A transverse incision was made through an avascular area of the anterior wall of the stomach. The bezoar was found lying high in the upper half of the stomach and was removed without difficulty (Fig. 2). There was no evidence of a gastric or duodenal ulcer.

The patient's postoperative course was uneventful until five days after the celiotomy. At this time the patient awakened in the middle of the night with a periumbilical pain, which, by morning, had localized to the right lower quadrant of the abdomen. There were rebound tenderness and muscle spasm in the right lower quadrant of the abdomen. The temperature was 101 F; the pulse was 90, and the white blood cell count rose to 18,000 per cubic millimeter. A diagnosis of acute appendicitis was made. An acutely inflamed appendix was removed through a McBurney's incision. Thereafter, the patient's course was uneventful, with discharge from the hospital on Dec. 11.

Fig. 3.—Appearance of the gastric bezoar removed approximately 10 days after the ingestion of persimmons.

Gross Pathology.—The specimen consisted of 120 gm. of fresh tissue with a diagnosis of foreign body of the stomach (wild persimmon bezoar) (Fig. 3). The bezoar was oval-shaped, measuring 9×5×5×6 cm. It was greenish-black, with an irregular, rough surface. The cut surface revealed a yellow-tan color with numerous seeds and debris (Fig. 4). No histological sections were made of the bezoar.

The appendix grossly and histologically was characteristic of acute appendicitis. No seeds were found within the lumen of the appendix.

Fig. 2.—Open stomach with the foreign body in view.

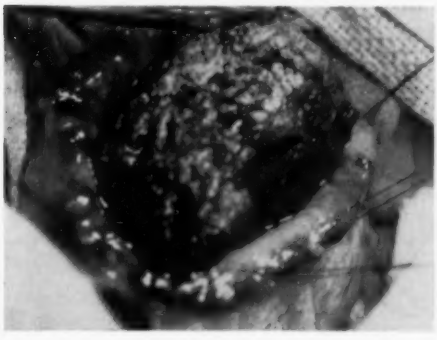

Fig. 4.—Cut section of the putty-like bezoar, exposing persimmon seeds and fragments of skins.

Summary and Conclusions

The case of a 49-year-old man is reviewed in which a preoperative diagnosis of a persimmon bezoar was made on the basis of the history of recent ingestion of persimmon fruit and the roentgen appearance of an obstructing foreign body in the stomach. Early surgical intervention resulted in removal of a gastric persimmon bezoar. No peptic ulcer was noted in the stomach. Recovery was complicated only by an attack of acute appendicitis on the fifth postoperative day. An appendectomy was accomplished without incident.

The roentgen diagnosis of a filling defect in the stomach, with the history of ingestion of persimmons, and the presence of a palpable abdominal mass should suggest the diagnosis of a persimmon bezoar.

The presence of a persimmon bezoar should be a consideration in the diagnosis of upper abdominal symptoms and obscure gastric lesions.

Early surgery is the most effective treatment in the management of these cases.

It is emphasized that a gastric persimmon bezoar may simulate carcinoma of the stomach. For this reason, it is obvious that no patient with a roentgen diagnosis suggestive of extensive carcinoma should be denied surgical exploration of a gastric lesion.

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Chylothorax as a Complication of Translumbar Aortography

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A recent excellent review by McAfee and Willson [3] of all the reported complications of translumbar aortography revealed no thoracic complications of the procedure. For that reason the following case is being reported.

Report of a Case

The patient, a 58-year-old white woman, was first seen in July, 1951, complaining of left upper quadrant abdominal pain of approximately 10 years' duration. Physical examination was essentially negative except for moderate left upper quadrant abdominal tenderness. No masses were palpated in the abdomen. The blood pressure was 130/80. A complete blood count and an urinalysis were normal. The examination of the stool for ova, parasites, and occult blood was negative. Gastric analysis showed no free hydrochloric acid after histamine stimulation. An intravenous pyelogram revealed no defects in the kidneys or ureters. A tentative diagnosis of irritable bowel syndrome was made, and the patient was placed on a therapeutic program to combat it. Because of persistence of symptoms, a retrograde pyelogram was done in December, 1951. It was essentially normal. In April, 1952, barium enema and upper gastrointestinal x-ray studies showed no abnormalities. In May, 1952, the pulsations of the abdominal aorta were noted to be prominent, and marked tenderness was noted over the abdominal aorta. In June, 1953, the patient's symptoms were still present. At that time examination revealed the abdominal aorta to be larger and more tender than it had been on previous examinations. Aortography was advised but was refused by the patient. She was seen thereafter at frequent intervals. In August, 1955, because of persistent symptoms and apparent increase in size of the abdominal aorta and continued tenderness of the abdominal aorta, aortography again was advised and again was refused. In May, 1956, the abdominal aorta was noted to be definitely palpable throughout its course and to extend to the left of the midline above the bifurcation, at which point it was very tender. However, no definite aneurysm was palpable. Because of persistent, unexplained symptoms, aortography again was advised and was accepted by the patient.

On May 4, 1956, aortography was performed under general anesthesia with intravenous thiopental (Pentothal) sodium. With the patient in the prone position, a No. 17 Huber pointed needle 6.0 in. (15 cm.) in length was inserted through a small stab wound made 8 cm. to the left of the spine of the first lumbar vertebra. The needle was directed medially and cephalad until a vertebral body was encountered. The needle was then backed off and advanced anterior to the body of the vertebra. The aorta was not immediately encountered. However, on the third insertion of the needle the aorta was entered. An x-ray exposure after injection of 5 cc. of 50% diatrizoate (Hypaque) sodium showed the needle to be in satisfactory position above the celiac axis. An aortogram then was made, using 30 cc. of 50% diatrizoate sodium. The aortogram showed slight elongation of the aorta with slight tortuosity to the left (Fig. 1). There was no aneurysm.

The patient was discharged from the hospital on the following day. She returned on the fourth day after aortography, complaining of substernal tightness, cough, mild dyspnea, and pain in the right side of the chest on deep breathing. There was absence of breath sounds in the lower half of the right chest. A chest x-ray showed moderate right hydrothorax and mild left hydrothorax (Fig. 2). A thoracentesis was done, and 1650 cc. of milky fluid was obtained. On May 12 a thoracentesis of the right chest produced 1900 cc. of milky fluid. Thoracentesis on May 16 produced 2500 cc. of the same type of fluid. The fluid obtained was sterile on culture. Microscopic examination of the sediment revealed neutrophils, eosinophils, and large numbers of histiocytes and lymphocytes. On standing, the fluid separated into an upper, creamy layer and a lower, milky layer. Between May 4 and May 16, the patient lost 7 lb. (3.2 kg.) of weight. On May 18 a right thoracotomy was performed. The chest was entered through the right eighth interspace; 2500 cc. of faintly blood-stained chylous fluid was removed from the chest.

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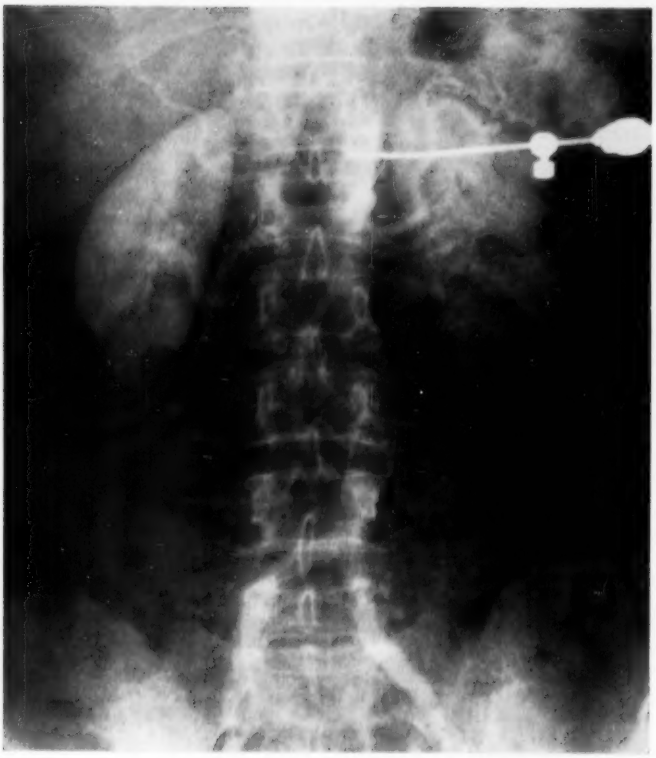

Fig. 1.—Aortogram showing needle in place above celiac axis. Slight lengthening and tortuosity of abdominal aorta. No aneurysm.

The chyle was found to be leaking from a tiny papilla in the parietal pleura over the ninth thoracic vertebra. After the mediastinal pleura was opened, the thoracic duct was found fairly easily. A tributary of the duct was found to have been partially severed and to be leaking chyle. Six hours prior to surgery, 4 oz. (125 cc.) of olive oil, emulsified with 1 gm. of a red dye (Sudan III), had been given by mouth. The chylous fluid coming from the thoracic duct was not colored by the dye. It was slightly milky in appearance. When the thoracic duct was occluded, the chyle flowing from the nipple-like opening over the ninth thoracic vertebra ceased entirely. The partially severed tributary of the thoracic duct was individually ligated with 000 nonabsorbable surgical suture U. S. P. (cotton). The thoracic duct itself was ligated with 000 cotton. The mediastinal pleura was loosely closed with absorbable surgical sutures. The chest wound was closed in layers. The chest was not drained. Convalescence was uneventful. When last seen, on Nov. 26, 1956, the patient had no difficulties with the chest, and a roentgenogram of the chest was essentially negative.

Comment

Physical examination of the patient usually will provide the information necessary before surgery in cases of aneurysm or arteriosclerotic occlusive disease of the abdominal aorta. However, aortography is advisable when the diagnosis is in doubt. It is also useful in some diagnostic problems of the urinary tract.

The needle used for injection should enter the aorta above the site of origin of the renal arteries in order to demonstrate the relationship of the aneurysm or the occlusive process to the renal arteries. It is well to have the needle enter the aorta above the origin of the celiac axis and superior mesenteric arteries in order to avoid direct injection of the contrast medium into these important vessels. The celiac axis arises immediately below the aortic hiatus of the

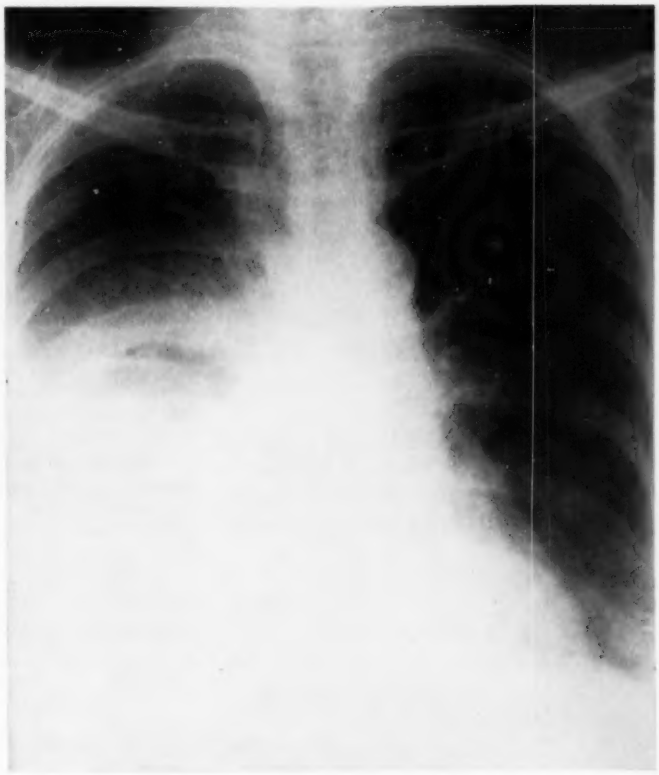

Fig. 2.—Roentgenogram of chest taken on fourth day after translumbar aortography. Right hydrothorax (proved by thoracentesis to be chyle).

diaphragm. Therefore, if the surgeon attempts to direct the needle into the aorta above the celiac axis, the needle almost certainly will enter the lowermost portion of the thoracic aorta. If the needle misses the aorta, it may damage other structures, especially the thoracic duct. The thoracic duct at this level traverses the aortic hiatus with the aorta and lies behind and slightly to the right of the aorta. It varies in diameter from 2 to 6 mm. In this position it is covered by a recess of the right plural cavity. There are many variations from this anatomical pattern. The thoracic duct is characterized by its frequent anomalies, as to both branches and course.

Injury to the thoracic duct is likely to result in chylothorax. In order to produce chylothorax, it is not necessary that the pleura be injured simultaneously. If the chyle does not have ready access to the pleural cavity, it pools in the retropleural space until it causes pressure necrosis of a small portion of the pleura. This usually takes three to seven days to develop.[2] The chyle then pours into the pleural cavity. Presumably this was the mechanism of chylothorax in the presently reported case.

Although conservative measures may eventually produce a cure, the protracted loss of chyle results in nutritional deficiencies. A direct surgical attack is usually necessary and immediately effective. Brewer [1] stated that the postponement of surgical treatment is no longer justified, that the greatest chance for success is to be found soon after the chylothorax is established, and that simple ligation is all that is necessary in most instances of perforation of the duct in the thoracic region.

Summary

A case is reported in which right chylothorax occurred as a complication of aortography. The needle used for injection lacerated a tributary of the thoracic duct behind and to the right of the aorta, just above the aortic hiatus of the diaphragm. Chylothorax occurred in four days. At operation, on the 14th day after aortography, the site of the damage to the duct was demonstrated. Ligation of the duct controlled the chylothorax.

Addendum

Since this article was submitted for publication, a similar case has been credited to Deterling by Crawford et al. (*Surg., Gynec. & Obst.* 104:129 [Feb.] 1957). Deterling, in a personal communication, stated the case to be the same one reported by Malufand McCoy (*Am. J. Roentgenol.* 75:533 [April] 1955). The case reported by us is the second case to require transthoracic ligation of the thoracic duct.

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Gigantic Ventral Hernias

A Report of Three Cases

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The two common types of ventral hernia in the adult are the umbilical and the incisional. The umbilical hernia as an acquired lesion is a defect in the linea alba at the level of the umbilicus, starting at the weakest point of the umbilicus—the superior portion of the original ring. It is associated with obesity and conditions that cause increased intra-abdominal pressure. The fascial defect varies in size but is usually disproportionately small as compared with the size of the sac. Even when the sac is small, as a rule, the defect is smaller. The sac may be so huge as to accommodate a large amount of intra-abdominal contents which manage to enter through a relatively narrow defect.

Incisional hernia is the consequence of a surgical procedure. The anatomic defect varies with the location. The relation between the size of the defect and the size of the sac in incisional hernias is not so constant as in umbilical hernias. Although the same type of disproportion and its attendant danger of incarceration take place in the two types, the other extreme is also encountered: a fascial defect through tissue loss so extensive that almost no fascial barrier remains in the anterior abdominal wall. The wall then consists mainly of skin, varying amounts of subcutaneous tissue, and peritoneum. Incarceration is not one of the problems in the diastasis-like hernia. When both a large fascial defect and disproportion do exist in an incisional hernia, the problem is truly great.

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When a ventral hernia is reducible, one can palpate the defect to ascertain its size. If the contents are chronically incarcerated, palpation for size is not possible; in that event, one can only estimate the size of the defect. In a large pendulous hernia, whether incisional or umbilical, it is probable that the fascial defect is relatively smaller, and that disproportion is potentially dangerous, for even in the absence of symptoms at the time of initial examination, it cannot be assumed that the condition will remain asymptomatic.

In addition to the size of the defect, the surgeon is concerned with the loss of right of domicile, the type of tissue to be repaired, and the prevention of immediate or delayed recurrence.

In the three cases reported herewith the patients presented with both emergency and elective problems, and chronic incarceration had been of long duration.

Report of Cases

CASE 1.—A white woman aged 68, known to have diabetes, entered the Cook County Hospital on Jan. 15, 1951, because of abdominal pain, distention, and constipation of several days' duration. A gallbladder operation had been performed 48 years earlier. A protrusion observed through the lower end of the scar a year postoperatively gradually increased in size until it became the massive ventral hernia that lay beside her in bed at the time of admission. Twenty-six years before, the patient had experienced an intestinal obstruction, of unknown etiology. At that time a transverse colostomy had been done through a right paramedian incision. The colonic stoma opened and closed spontaneously, so that the patient had approximately three spontaneous bowel movements by rectum in a year. In 1950, one year before the present admission, the patient again had an acute intestinal obstruction, diagnosed as having

been caused by an incarceration of the colonic stoma. Several fistulous openings were around the colonic stoma. Examination having revealed a normal colon, the colonic stoma was closed, and the fistulas were excised.

The observation of the huge ventral hernia was recorded at that time, but the operative note stated: "To replace this large ventral hernia coincidentally may end in disaster for the patient. The defect is too big to repair. Everything is matted together. Unwise to attempt." It was not recorded whether future repair was considered to be feasible. As will be seen, successful subsequent repair proved both possible and indicated.

On admission, the hernia was generally tender, but rebound tenderness was not present. The patient was placed on a stretcher; the hernia lay on the x-ray table beside her. The roentgenogram showed the dilated small bowel within the sac. A diagnosis was made of incomplete small-bowel obstruction. The patient responded to conservative decompression; oral intake was possible during preparation for an elective repair. An elliptical incision was made down to the fascia and neck of the sac, which was then opened; the matted contents were restored to normal relationship in the abdominal cavity. The contents consisted of the distal portion of the stomach, the duodenum, and all the small bowel and its mesentery, as well as the entire large bowel and a distinct mesentery, exclusive of the rectosigmoid and rectum. This was not a sliding hernia; it appeared that the free mesentery of the large colon was not a congenital failure of fixation but an acquired status. The fascia surrounding the defect was in a remarkably good state. Closure was secured by through-and-through double strands of steel wire. Drains were placed down to the fascia; the skin was closed. The patient remained well for several years afterward, when follow-up examinations were discontinued.

Case 2.—A white woman aged 77 was admitted to Illinois Masonic Hospital on Feb. 13, 1953, because of four days' failure of bowel movements and continuous vomiting for 48 hours. The patient was in shock on admission, with a blood pressure of 40/0. A huge umbilical hernia was observed, which was later learned to have been of 43 years' duration. The patient had worn a special garment in order to get about; apparently the hernia had otherwise been asymptomatic.

By Levin suction, 2600 cc. of coffee-ground material was obtained, and an equal amount was vomited. Hyperactive bowel sounds were heard in the hernia. The clinical impression was that of gastric dilatation or a possible high intestinal obstruction, and an enormous umbilical hernia with chronic incarceration. The patient was dehydrated; hypochloremic alkalosis and oliguria were complicating. Levin decompression, adequate fluid, and electrolyte therapy improved the patient's general condition and increased the urinary output. After several days, graduated oral intake was possible. Improvement continued, and barium x-ray studies were undertaken with caution. The roentgenologist reported that at least the distal half of the stomach, most of the duodenum, and the entire small bowel and colon as far as the rectosigmoid were within the hernial sac. Evidence of chronic obstruction in the third portion of the duodenum resulted from extrinsic narrowing. A constriction of the sigmoid from extrinsic narrowing was also observed. Surgery was elective. At operation the contents were observed to be exactly as described roentgenologically.

The weight of the contents had caused traction at the duodenojejunal junction, with consequent angulation and chronic partial obstruction of the duodenum, which was dilated and thickened. The defect itself was approximately 18 cm. at its greatest diameter, but the fascia about this area was extremely thin. The viscera were returned to the abdomen. A Mayo type of repair was accomplished. Tantalum mesh served as reinforcement. Drains were placed down to the fascia. The patient made an uneventful recovery. One month later, while at home, she experienced a pulmonary infarct, but recovered and remained well without recurrence until the time of her death, from unrelated causes.

Fig. 1 (Case 3).—Preoperative view of gigantic pendulous hernia. Note healed scar of wound through which patient observed intestinal action during healing process.

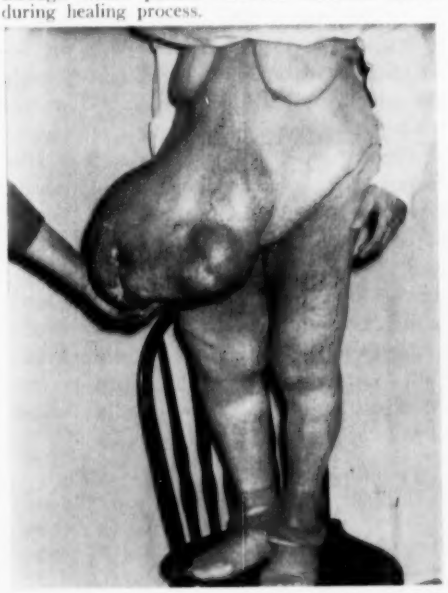

Fig. 2 (Case 3).—Preoperative view. Orange-peel appearance of skin in most dependent portion of hernia; healed scar.

CASE 3.—A woman aged 59 was admitted to the Women and Children's Hospital on March 7, 1956, for elective repair of a gigantic ventral hernia (Figs. 1 and 2). The patient, who was 5 ft. (152.4 cm.) in height, at one time had weighed 270 lb. (122.4 kg.), but weighed 154 lb. (69.9 kg.) when admitted. She had had an umbilical hernia repaired 27 years before admission. The hernia, which recurred a year postoperatively, had been neglected and had grown to the proportions present on admission.

Orange-peel changes in the skin of the most dependent portion of the hernial sac had become ulcerated at one time, after a fall. The patient reported having been able to see intestinal loops through the ulcerated area, which eventually healed. Except for the unwieldiness of the hernia, restricting the patient's activity, the condition was apparently asymptomatic.

An elective repair was accomplished through an elliptical incision made down to the fascia and the neck of the sac. The defect was a relatively small one (Fig. 3), although the fascia about it was greatly thinned. The contents of the sac itself were similar to those in the other two cases (Fig. 4). The presence in the sac of dilated and collapsed loops of small bowel suggested an incomplete obstruction of the small bowel, notwithstanding apparent absence of symptoms.

Fig. 4 (Case 3).—Contents of sac. Note appendix and ascending colon; transverse colon, above, hiding lower portion of stomach and duodenum, and small bowel and mesentery, hiding descending colon.

Surgalloy (stainless steel suture, multistrand) was used in a Mayo type of repair, and tantalum mesh as reinforcement. Drains were placed down to the fascia. The patient made a good recovery (Fig. 5). Postoperatively the respiratory rate increased; slight cyanosis appeared. Evidently the patient was not aware of dyspnea. The symptoms soon disappeared. Roentgenograms revealed a bilateral high-riding diaphragm, which gradually receded to normal. Homologous serum jaundice was a later development, from which the patient likewise recovered.

Comment

Two of the three patients whose cases are reported here were admitted to the hospital because of an acute and critical illness. How much and in what manner the gigantic hernia contributed to the illness were not immediately apparent. The third patient came

Fig. 3 (Case 3).—Small size of defect in proportion to hugeness of sac.

Fig. 5 (Case 3).—Nine days postoperatively. Note poor tissue turgor after loss of weight.

to the office to ask whether anything could be done for her and thus was a candidate for an elective procedure.

In each case extraordinary unwieldiness of the hernia restricted activity, and the appearance was cosmetically unsightly; moreover, in each case complication proved to be due to the hernia. In two cases the complication was an acute intestinal obstruction; in the third case complications were serious, stasis-producing changes in the dependent portion of the skin of the hernia and gross pathologic evidence of a partial obstruction of the small bowel, notwithstanding the absence of referable symptoms. Skin complication of the type that this patient experienced is not unknown. Some cases have eventuated in rupture, with peritonitis and death.*

In all three cases chronic incarceration had been of long duration. The sac in each case contained organs that are normally mobile, as well as organs that are capable of developing mobility. Thus, in each instance the contents included the distal portion of the stomach, the duodenum, the head of the pancreas, the entire small bowel and mesentery, and the large bowel with a distinct mesentery, but excluding the rectosigmoid and rectum. The mechanism by which this mobility is brought about appears to be traction. The sac in each instance was enormous, as can be judged by the contents, and in each the hernia was pendulous. The size of the sac, however, did not represent the size of the defect, which in the three cases was relatively small. This characteristic relationship is apparent in Figure 3. The fascia about the defect was surprisingly satisfactory in one case but understandably poor in the other two cases.

The factors of decompression, anesthesia, oxygen, administration of antibiotics and fluid, and electrolyte therapy were each carefully assayed for each patient.

The principles of repair are basic, as they are the same regardless of the size of the hernial sac or the size of the defect. In the case of a large defect a prosthesis other than supportive may be required, but this was not necessary in any of the cases reported here.

An elliptical incision was made around the sac down to the fascia and the neck of the sac. The sac was opened at the neck, and the contents were isolated. The contents, severely distorted, were in each case densely adherent one part to another and to the sac. Although aware of the problem of the right of domicile, in no instance did I attempt preoperatively to increase the capacity of the peritoneal cavity by pneumoperitoneum [1] or phrenicectomy [2] or relaxing incisions through the fascia at surgery. Those methods must have their merits, for the problem of accommodation to the increased intra-abdominal pressure is real. It may be that, because the patients under discussion were at one time obese but were not obese at the time of operation, placing the operating table in an inverted-jacknife, or V, position was sufficient to facilitate the return of the viscera to the abdomen, with satisfactory closure and favorable postoperative course.

Either nonabsorbable suture of steel wire or Surgalloy was used in repair; tantalum screen mesh was placed as reinforcement in the two instances of poor fascia surrounding the defect. In all cases drains were placed down to the fascia.

The first patient had an uneventful course. The second patient experienced a pulmonary infarct a month after surgery but recovered. The third patient, although subjectively comfortable and apparently unaware of dyspnea, had a slightly increased respiratory rate [3] and a suggestion of cyanosis of the lips, as well as a moderate elevation of the diaphragm, as seen roentgenographically. At the time of her discharge, 10 days later, she had completely accommodated. Three months later, she was hospitalized because of homologous serum jaundice, from which she recovered. Within a year postoperatively, for

* Two cases known to author: one, personal observation at Cook County Hospital; the other, personal communication to the author by Dr. Eloise Parsons.

the first time in 26 years, the patient was gainfully employed. Hernia has not recurred to the date of this writing (January, 1957).

In balancing the factors in the problem of massive hernia, as in all surgical conditions, one weighs the risk of the continuing disease against the general health of the patient and the magnitude of the surgical procedure indicated. Massive ventral hernia is a disease of neglect—usually, but not always,[3] long-term neglect, which permits time for their development. The durations in the cases cited were 47, 43, and 26 years, respectively. In cases covering so long a span the disease inevitably brings with it associated geriatric problems—at the very least, the problem of physiologic reserve.

A history of long-standing disease does not necessarily mean that the hernia is innocent of complication. Its presence does invite complications, such as intestinal obstruction and serious stasis-producing changes in the skin. It is the disproportion between the size of the sac and the size of the defect that predisposes to complication. The defect itself in the cases under discussion was 18 cm. at its greatest diameter.

In all three cases the sac contained organs that are normally mobile, as well as organs that can develop mobility. The mechanism by which this mobility is brought about appears to be traction.

A hernia should not be allowed to become gigantic in the first place; but when one is present, unless strong general contraindications prevail, repair is certainly advisable. Principles of operative technique are the same whether the hernial sac is small or large. The relatively small size of the defect in the present cases made repair feasible.

Accommodation to the increased intra-abdominal pressure on replacement of the viscera was possible without special preoperative measures, such as phrenicectomy prior to hernioplasty, or preoperative pneumoperitoneum, or relaxing techniques—all of which doubtless have merit.

Postoperative morbidity does not suggest undue risk in surgical intervention for gigantic hernia, even in elderly patients.

30 N. Michigan Ave. (2).

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Gastric Ulcer, a Surgical Problem

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Ulcerating lesions of the stomach are of frequent occurrence, and the possibility of their being malignant can never be ruled out except by microscopic examination. They are not infrequently associated with serious complications. Medical treatment of such ulcers has proved ineffective in a high percentage of cases. Gastric resection, on the other hand, can be done with a low mortality, and end-results with few exceptions are most gratifying. The purpose of this presentation is to submit evidence to show that these statements are true and to urge that all ulcerating lesions of the stomach be considered a surgical problem from the moment of diagnosis.

A comparison of the results of medical versus surgical treatment of gastric ulcers needs to be often repeated, not only to surgeons, especially those not primarily interested in gastric surgery, but particularly to internists, gastroenterologists, and general practitioners, who too frequently are reluctant to relinquish the care of patients suffering from such lesions.

While statistics abound with articles extolling the virtues of medical therapy for gastric ulcers, there are comparatively few observations to be found recording large series of cases observed over a long period of time to determine what the ultimate curability rate by this method of therapy has been. The following articles are cited because they have been enlightening to me, and if they reflect the usual outcome when such lesions are treated conservatively—and I have no reason to doubt that they do—medical treatment has proved to be woefully inadequate.

Swynnerton and Tanner,[1] in 1953, reported treating 498 gastric ulcers, with a follow-up period of 5 to 12 years. Approximately one-half of these ulcers were treated medically; the other one-half were treated by gastric resection. These authors found that medical treatment will keep gastric ulcers healed in only one-fourth of the milder and earlier cases. Of those treated surgically, results were satisfactory in 80%, moderately satisfactory in 10%, and poor in 10%. Poor results were generally found to be due to conditions not directly related to the ulcer.

Cain, Jordan, Comfort, and Gray,[2] reporting from the Mayo Clinic in 1952, stated that in a recent five-year or longer follow-up of 414 small ulcerating lesions of the stomach treated medically, relief of symptoms was satisfactory in only 20.5% of cases, cancer was present or developed in 10.4% of the total group, and ultimately medical management was abandoned for surgical treatment in 33.8% of the cases.

Martin and Lewis,[3] in 1949, in an experience with 96 verified gastric ulcers, found that 56% had been under medical treatment for 10 years or longer and were still active. Natvig and associates,[4] in 1943, in a three-year follow-up of 152 cases, found 44% symptom-free, but six and one-half to nine and one-half years later the percentage had dropped to 22. Malmros and Hiertonn,[5] in 1949, followed 193 gastric ulcers treated medically for 7 to 10 years and found that 36.5% showed favorable results, but not all of the patients were free of symptoms. Banks and Zetzel[6] (1953) followed 48 medically treated gastric ulcers which they believe received the usual type of medical supervision. Of these, 4 had been followed for 15 years; 7, for 10 to 15 years; 20, for 5 to 10 years, and the remainder, for an average of 2½ years. Of the 48 patients, only 11 had remained free

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From the Straub Clinic.

of ulcer symptoms throughout the follow-up period, and 8, or 16.6% of the 48, have died of verified carcinoma of the stomach. Hayes,[7] from the department of surgery of Yale University, in October, 1955, reported on the gastric ulcer problem. During the 20-year period from 1929 to 1949, a study had been made of 899 patients with peptic ulcer symptoms of less than six months' duration in whom a final diagnosis of gastric ulcer or cancer was made. Of these lesions, 472 were diagnosed with certainty as being gastric malignancy and 427 were diagnosed as undoubtedly being benign. One hundred ninety-six of these, with no more than four weeks' medical management, were operated upon, and in 28.6% cancer was found. Ninety per cent of the cases, whether benign or malignant, were symptomatically improved by well-supervised medical treatment. The five-year survival rate for gastric ulcers treated for not more than four weeks which proved to be malignant on microscopic examination only was 66%, not crediting a 5.2% death rate from nonassociated disease. In 5% of the cases reported by the pathologist to be benign, death from adenocarcinoma occurred, the stomach being the presumed primary site. This observation emphasizes the necessity of examining all gastric ulcers by serial section before concluding that they are benign. Of the 231 cases in the medical series, 42% required operative treatment, and only 1 in 3 was "cured" for a period of five years. The interesting and important observation was made that when operation was done for intractability or recurrence within five years, 25% to 30% of the cases were found to be malignant. Palmer, of Chicago, a strong advocate of conservative treatment of gastric ulcers, in discussing this paper, admitted that probably 40% to 50% of medically treated gastric ulcers do recur.

The most serious deterring factor causing one to hesitate to advise medical treatment of any ulcerating lesion of the stomach is always the very real possibility that the condition is malignant in nature, regardless of its seeming benignancy after all methods of investigation now available have been used. The percentage of error in concluding that such lesions are benign, when later shown to be malignant, varies no doubt in proportion to the experience and diagnostic acumen of the investigators, but I dare say it remains at least in the neighborhood of 10% in the hands of most medical men responsible for the care of the majority of these patients.

Allen,[8] in 1951, stated that "gastric ulcer visible by x-ray and characteristic in every way of a benign lesion will prove to be cancer in at least 10 per cent of all cases." Marshall,[9] of the Lahey Clinic, in 411 cases of gastric ulcer that came to surgery because malignant disease could not be excluded clinically or because the ulcer recurred or failed to heal, reported an incidence of cancer of 15.8%. Lampert, Waugh and Dockerty,[10] of 550 resected ulcers thought preoperatively to be benign, found that 13% were malignant. Cole,[11] in a recent panel discussion of ulcers and cancers of the stomach, stated that most articles commenting on this subject admitted a 10% to 12% error.

Aside from the possibility of cancer, there are other very potent reasons recommending surgery in the presence of such lesions. Hemorrhage, perforation, pyloric obstruction, physical suffering, and loss of efficiency and time from work are frequent complications of the patient undergoing medical treatment, particularly in the patient unable by force of circumstances to adhere to a strict medical regime. Surgical treatment, on the other hand, is usually limited to a short, decisive encounter, ending in a permanent satisfactory result.

If surgical measures are to be recommended over a conservative approach, there must be substantial evidence to prove its superiority. To me, at least, it is not a difficult task to accumulate such evidence. Medical literature and expressed opinions of surgeons on many occasions, and our own experience in particular, prove that gastric resection for benign ulcer of the stomach is one of the most satisfactory op-

erations in abdominal surgery. Surgical mortality is low; complications rarely occur, and end-results, with few exceptions, are satisfactory. Walters [12] has recently stated that gastric resection for gastric ulcer, in his hands has resulted in 95% excellent results, and Kiernan [13] had only one unsatisfactory result in 162 gastric resections for gastric ulcer. The mortality following resection for benign gastric ulcer in clinics familiar with the problem is low. In Marshall's 411 cases, it was 2.2%, and, as he stated, it is given in the literature as being from 2% to 5%. In our last 294 consecutive cases, we have lost 2 patients in the postoperative period.

Medical men and some surgeons who are not familiar with the problems of gastric surgery confuse the results to be expected following surgery for duodenal ulcer with those following resection for gastric ulcer. Whatever the variation in the etiology of these two conditions may be, the end-results in any large series of cases are always better following surgery for gastric ulcer. The principal reasons for this difference in results are these: (1) The duodenum in gastric ulcer is usually free of involvement and therefore can be closed more securely than in many cases of duodenal ulcer; (2) recurrent ulcer following gastric resection for gastric ulcer is rarely seen, and (3) it is not only unnecessary but unwise to resect a large part of the stomach when dealing with a gastric ulcer.

It is my belief—though contrary to the belief of some others—that the dumping syndrome or postgastrectomy symptoms are largely dependent upon the amount of stomach resected. For this reason, I believe it is undesirable to resect more than 60% of the stomach when surgery is done for benign gastric ulcer if removal of more can be avoided—and it usually can be.

It has been the practice of most physicians in the past—and it continues to be the practice of too many in the present—to institute medical measures for a varying period of time in the treatment of gastric ulcer to see whether symptoms improve and the ulcer disappears. In our earlier experience with this problem, we followed this method of procedure. In some of the cases, the results were gratifying and the patient escaped operation. In other instances, the symptoms improved for a time, and the crater diminished in size or disappeared, even though the ulcer later proved to be due to cancer. When some of these patients returned, examination left little or no doubt as to the nature of the patient's trouble and equally little doubt as to the value of any form of therapy.

Ravdin,[14] in discussing this phase of the problem, said:

> We must admit the possibility that up to 10 per cent of benign gastric ulcer patients may eventually develop gastric cancer at the site of the benign ulcer. Because of this and because of the record of admitted diagnostic errors at every institution, and because the three to six, or even eight, weeks' trial of medical therapy so frequently stretches into months or even years, we believe that the therapy of gastric ulcer should be regarded primarily as a problem for the surgeon, provided the surgeon is sufficiently able and experienced in gastric surgery to perform radical gastric resection with a satisfactory small operative risk.

Ochsner and Blalock [16] had this to say:

> Because of the impossibility of differentiating between benign and malignant ulcers by all of the presently available methods of diagnosis and also because of the possibility that an ulcer or a healed ulcer scar in the stomach may be a precancerous lesion, we are convinced that all gastric ulcers should be excised and that none should be treated conservatively.

A study of small gastric cancers by Comfort and associates,[15] of the Mayo Clinic, reported in 1954 sheds considerable light on the subject of ulcerating lesions of the stomach that are difficult or impossible to determine as being benign or malignant. They studied 226 small gastric adenocarcinomas 4 cm. or less in greatest diameter which had been treated by resection in the years 1940 to 1945, inclusive. They found these significant facts: (1) These small cancers comprise one-fourth of all gastric cancers for which resection was performed in these years; (2) they consisted of a slightly higher percentage of lower grades

of malignancy; (3) they showed a smaller incidence of metastases; (4) by their symptoms, these small cancers tended to simulate benign gastric ulcers; (5) their malignant nature was recognized roentgenologically in only about one-third of cases, and (6) the hospital mortality rate was lower and the five-year survival rate higher. The authors further stated that, while this gastric cancer form is the most favorable for surgical treatment, unfortunately it is the one most frequently treated medically in the belief that it is a benign ulcer.

Since no one can ever be sure that any given ulcer is benign until it is adequately examined by the pathologist, the question of how radical the resection should be always comes up for consideration at the time of operation. When the lesion appears grossly benign, removing lymph nodes adjacent to the ulcer for frozen section establishes the diagnosis when they are positive for metastasis but leaves one in doubt as to the nature of the lesion when they are negative. A portion or the entire ulcer may be excised for study, but this has the possibility of disseminating cancer cells. The procedure is time-consuming and undesirable from the standpoint of a clean operation. Opening the stomach and biting out portions of the wall of the ulcer for microscopic study has been advised, but this has the same undesirable features and very early cancers may be missed. We have tried doing a conservative resection and, if the ulcer showed evidence of malignancy, attempting then to do a more radical resection. This has not seemed to be a very sensible answer to the problem, either. It seems to me that in these doubtful cases one should remove what appears to be an adequate amount of stomach around the ulcer, and the regional lymph nodes as widely as possible without removing the greater omentum, the peritoneum over the pancreas, and, as some suggest, the spleen and other structures. It has been shown repeatedly that if metastasis has occurred beyond the point of this suggested removal, comparatively few people survive for five years, regardless of how radical an operation is done. When, as occasionally happens, the pathologist, after a study of permanent sections, reports several days later finding an area showing malignancy, I believe it is unwise to subject the patient to further surgery. In discussing this problem, Ravdin agrees with Grimes and Bell [17] that, because of the number of errors that are made in preoperative diagnosis and further contributed to by the surgeon at operation, and even by the pathologist on gross examination, the operation performed should as a rule be the same procedure as that for a known cancer. It has been my experience that if one becomes too radical in cleaning out the lymph nodes along the lesser curvature up to the esophagus, with resection of the left gastric artery and removal of the spleen, high resection of the stomach becomes necessary in order to maintain an adequate blood supply, and this is undesirable if the lesion proves to be benign.

The type of surgical resection used in our series of cases has been for the most part the Billroth II operation, using the modified technique of Polya-Hofmeister with retrocolic anastomosis. In the past few years, my younger associates have become somewhat partial to the Billroth I type of resection, but I have not been tempted to change, since results with the Billroth II procedure have been so satisfactory. The report last year by Waltman Walters before the American Surgical Association of seven recurrent ulcers following Billroth I resection in 135 cases of gastric ulcer makes me even more reluctant to adopt this type of procedure.

Numerous examples could be cited in our own experience to show the difficulty, or, rather, I should say the impossibility, in most instances of differentiating the small ulcerating lesion of the stomach that is malignant from one that is benign. The following is a typical case report.

A Japanese man, age 49, was first seen at the Straub Clinic on March 6, 1956, complaining of epigastric distress relieved by eating, of two months' duration. X-ray study of the stomach showed a small penetrating gastric ulcer of the

lesser curvature, middle third, just proximal to the angle (Fig. 1). Believing that the lesion in all probability was benign, a conservative resection of the stomach was done, and the pathologist studied several frozen sections of the ulcer without finding any area suggestive of malignancy. Later, after more thorough study of permanent sections, a small carcinomatous area was demonstrated (Fig. 2). No evidence of metastasis to regional lymph nodes was found. This patient, I believe, has a good chance of being cured.

How, may one ask with due propriety, can the diagnosis of cancer be made preoperatively with any degree of frequency in such lesions as these? X-ray and fluoroscopic examination is not the answer, and neither can reliance be placed on gastroscopic examination and cytological studies. The shortcomings of these methods of investigation have been discussed in a previous publication [18] and will not be dealt with again here. Certainly, comparatively few patients survive any appreciable length of time by any method of treatment when a clinical diagnosis of cancer of the stomach is made, and the only cases that offer much hope for cure or long amelioration are those found by the pathologist on microscopic examination.

Fig. 1.—Small ulcer, lesser curvature of the stomach, thought clinically to be benign.

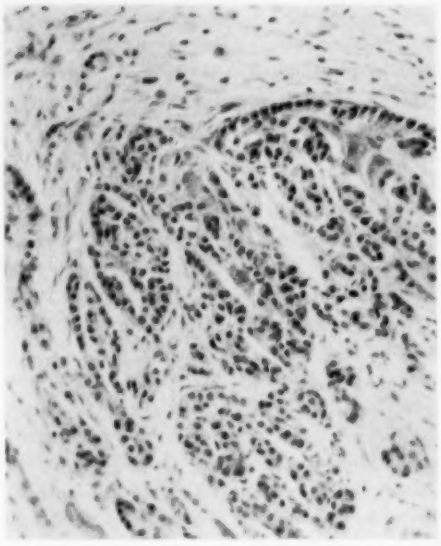

Fig. 2.—Small area of carcinoma found in wall of ulcer only after a number of sections had been examined.

Comment

It would seem that the data cited, which have been accumulated by men for whose integrity and surgical judgment we have the greatest respect, would be sufficient to convince the most skeptical that there is no place for the conservative treatment of ulcerating lesions of the stomach if the patient is an adequate surgical risk and he is to be taken care of by those skilled in handling such problems. To the experience of others, I should like to add the experience we have had at the Straub Clinic with 294 benign gastric ulcers and, during the same period, with 310 gastric cancers that have been treated surgically.

In these 294 consecutive gastric resections for benign ulcer, there have been 2 deaths, one attributable to disruption of the incision, the other from perforation of the residual stomach, the result of an anomalous and insufficient blood supply. Both deaths were preventable. While postoperatively some of these patients have complained of symptoms that may be classified under the heading of the dumping syndrome, with the usual methods of treatment and lapse of

time all have had these symptoms clear up so far as I can determine, with one exception. To my knowledge, only one patient has had a recurrent ulcer.

In our own experience, we cannot determine how many ulcers that appear to be benign are found to be malignant after resection or what success is to be achieved by medical therapy, for our attitude is that all ulcerating lesions of the stomach are malignant until proved otherwise. The fact remains that in clinics where an effort has been made to differentiate benign and malignant lesions, the incidence of error at best continues to be around 10%.

While the most convincing argument for immediate resection of all ulcers of the stomach is based on the possibility of the ulcer now being malignant, one cannot dismiss the possibility that the ulcer may undergo malignant degeneration in the future. The frequency with which this may occur has been much debated in the past, and there seems to be no method at present of accurately determining this point in the future. Many patients give a long history compatible with the presence of a benign lesion who ultimately develop cancer of the stomach, and in some instances a crater has been demonstrated a number of years previously in the same area in which the cancer has arisen. It has been the experience of those observing a large series of gastric ulcer patients over a long period of time that the longer this period of observation is carried out, the greater the percentage of patients that ultimately develop cancer of the stomach. It seems strange to conclude that an organ so susceptible to the development of cancer as the stomach would not be influenced to become cancerous by the presence of a chronic irritating process when this has been recognized as a predisposing factor to the development of cancer in all other parts of the body. Marshall, after reviewing the literature relative to this subject and incorporating his own clinical impressions, came to the conclusion that probably 5% of benign ulcers may ultimately undergo malignant degeneration. Ravdin places the figure around 10%, while Marcus [19] believes that it lies somewhere between 9% and 17%.

In Hawaii, we have long recognized that cancer of the stomach occurs in the Japanese about two to two and one-half times as frequently as it does in Caucasians. A five-year study was made recently of the incidence of benign gastric ulcer in these two races so diagnosed on discharge from the Queen's Hospital and St. Francis Hospital. During this time, 66,904 patients of these two races were discharged from these hospitals, in 297 of whom a diagnosis of benign gastric ulcer had been made. A diagnosis of benign ulcer was made one and one-half times as frequently in Japanese as in Caucasians. These two races were nearly equally represented. While statistically such a small series of cases proves nothing, it does suggest that benign ulcers of the stomach occur more frequently in Japanese than in Caucasians and may possibly be a factor in accounting for the high incidence of gastric cancer in this race. Further investigation of this subject, particularly in Japan, might bring forth some interesting observations.

The literature that has been cited dealing with conservative handling of gastric ulcers shows that from 50% to 75% of the cases, even after long periods of observation, are not cured. The longer the observation, the poorer are the results and the higher the incidence of gastric cancer. Even Palmer, an enthusiastic advocate of medical therapy of such lesions, admits that from 40% to 50% of such cases recur. Everyone, even the most conservative, apparently agrees that all recurring ulcers should be subjected to gastric resection because such ulcers are found in a very high percentage of cases to be carcinomatous.

The reasons up to this point for concluding that all gastric ulcers should be resected without delay to me seem valid, and I fail to see how anyone can advance sound argument to the contrary. For those who persist in believing in conservatism, additional evidence can be brought forth to emphasize

the potential dangers that accompany conservative treatment of such ulcers.

Everyone realizes that gastric ulcers at times do bleed, at times so alarmingly that operation seems indicated, and that following either surgery or conservative treatment there is an appreciable mortality. The same can be said for perforation of such ulcers. How much better it would have been to eliminate such ulcers before such complications had occurred, which always jeopardize the patient's survival!

If, as has been shown, such ulcers fail to remain healed in at least 50% of cases, there must be periods in which the patient is mentally and physically handicapped, contributing to inefficiency in his occupation and to his lack of enjoyment of life. One of the greatest rewarding experiences in the life of those doing abdominal surgery is the gratitude shown by such patients once they have been relieved of an ulcer that has been responsible for years of recurring suffering and disability.

Summary

In conclusion, I submit the following reasons for believing that all ulcerating lesions of the stomach are surgical problems from the moment of diagnosis:

1. Medical treatment has proved unsuccessful in a high percentage of cases.

2. At least 10% of all ulcers of the stomach that appear to be benign by all diagnostic measures now available prove to be malignant. The more intractable and the more frequently they recur, the more frequently they are found to be malignant.

3. Medically treated benign gastric ulcer has the possibility of undergoing malignant degeneration. Aside from cancer, untreated gastric ulcer may be associated with other serious complications.

4. Gastric resection for gastric ulcer can be done with low surgical mortality, and end-results, with few exceptions, are satisfactory.

5. Surgery for cancer of the stomach offers little hope for cure or long survival except when confined to the stomach or the immediate regional lymph nodes. These favorable conditions are rarely found except when the ulcer has the clinical characteristics suggestive of benignancy.

Straub Clinic.

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Infusion Treatment of Shock

Alkali and Acid in Shock Treatment

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The existing situation in the fluid therapy of shock has been accurately summarized by Wiggers.[1]

It is generally suspected that the beneficial effects of sodium chloride do not depend solely or largely on its ability to restore plasma volume. It must be due to the action of the sodium or chloride ions or of the NaCl molecule.

Illustrative of the first sentence is the superiority of saline over plasma [2-5] or dextran solution.[6] The problem of the second sentence is explored in the present paper.

Methods

Tourniquet shock, which was first standardized in rats,[2] was produced in dogs by tight constriction of both hindlegs as high as possible with heavy rubber bands or 6 mm. tubing. Anesthesia was induced with pentobarbital (Nembutal) intravenously or intraperitoneally. The animals were awake toward the end of the ligation period, when the limbs had lost sensation. Such constriction for five hours caused death within 1 to 5 hours after tourniquet removal in untreated animals or after intervals up to 45 hours in animals receiving various infusion fluids. Permanent survivals of a few animals in the experience of my colleagues and myself [2] or of others [6] were explainable by too low or too loose placement of the tourniquets. If desired, the shock can be intensified by waiting an hour or more after tourniquet removal before beginning treatment. In the experiments with hemorrhagic shock, one or another of the Wiggers methods [1,9-11] was employed.

Blood volume in a correlated investigation [6] was estimated with the Evans blue (T1824) method, but the parallelism with hematocrit and plasma protein readings was close enough to permit depending on these latter values for the present purpose. These and other analyses were done with standard technique by Mr. Frank Scudero, chemist at New York City Hospital. The organic effects were studied in pathological examinations by Dr. James R. Lisa of tissues from these and other experiments.[12]

From the New York City Hospital, Welfare Island.

Organon, Inc., furnished the heparin solution (Liquaemin Sodium) used in all the hemorrhagic shock experiments.

Rat Experiments

For brevity, experiments on 76 rats with four-hour ligation of both hindlegs will merely be summarized as to results of various solutions given by stomach or subcutaneously or intraperitoneally. Plain saline gave the longest survivals. The addition or substitution of alkali (sodium bicarbonate from 0.4% to 2.0%, sodium lactate M/6 in various quantities, and Hartmann's lactate-Ringer solution) shortened survival roughly in proportion to the quantity of alkali. Various phosphates added to saline, each 0.75%, gave results as follows: shortest survival with trisodium phosphate (reason unexplained); next shortest with Na_2HPO_4; longest with NaH_2PO_4. Ammonium chloride 1% in saline gave much long survival than ammonium acetate 1%. Stomach doses of 0.2% HCl in saline gave much longer survival than any of the alkalis. It being known that sodium is irreplaceable, the added impression was gained that any substitution of chlorine is also detrimental. The results contravened prevailing views of the relative effects of acid and alkali in shock.

These suggestive findings were not expanded into a statistical series because of various known differences between small rodents and larger species, including man. (*a*) Rats at the point of death from tourniquet shock are not revived by plasma or saline but are resuscitated only by whole blood.[2] (*b*) Fatality from visceral shock

in rats is not reduced but is increased by low temperature.[13] (*c*) Serum by stomach or saline intraperitoneally is as effective as intravenous administration in mice,[22] but neither statement holds good for severe shock in dog or man. Results of shock experiments in dogs have always proved reliable clinically in every detail.

The earlier experiments showing the superiority of saline over plasma led also to the following deduction[3]: "The results in shock are, therefore, attributed distinctly to the chloride of sodium until some other sodium compound can be proved similarly effective." The prevailing wide vogue of alkaline salts derives from a long history.[14-20]

Sodium bicarbonate was rejected by Cannon[21] in spite of its pressure-raising influence, and occasional later suggestions in behalf of it did not receive adoption. Plausible theoretical arguments for giving alkali are (*a*) to supply sodium without fixed anion, (*b*) to combat the apparent acidosis of shock, and (*c*) to protect kidney function. Organic compounds convertible into bicarbonate have come into widespread use, chiefly the lactate, on the strength of Rosenthal's experiments in mice.[22] An official publication of the U. S. Public Health Service[23] suggests that shocked patients drink a solution containing 3 or 4 gm. of sodium chloride and 2 or 3 gm. of sodium citrate, per liter, or perhaps substitute sodium bicarbonate for the citrate.

> Whenever profound peripheral circulatory collapse is present, the intravenous route of administration must be used until peripheral blood flow has been reestablished. The salt solutions that we have found most satisfactory for this purpose are Hartmann's solution . . . or plasma.

Dog Experiments

Controls are furnished by five experiments with isotonic saline, as illustrated in Table 1. The actual background of such controls comprises more than 50 dogs treated with variations of this method since the originally published experiments.[2,3] Because of the natural tendency to recovery in milder shock, the severest shock must be insisted upon for decisive comparisons of different fluids. The usual survivals of 36-45 hours with proper use of isotonic saline cannot be equaled with plasma[2,3] or

TABLE 1.—*Isotonic Saline for Five-Hour Tourniquet Shock in Male Dog*

Time, Hr.	Procedure Condition	Blood						
		Hematocrit, %	Plasma		Blood Pressure, Mm.	Urine Cc.	Hindquarters, Vol. Cc.	Body Weight, Kg.
			Protein, Gm. Per 100 Cc.	CO_2, Vol. %				
Before tourniquet removal		40	6.3	46	110	..	3450	7.3
After tourniquet removal, 1 hr.		52	7.1	43	80	..		
2½	400 cc. saline in jugular vein	38	5.7	..	55, rose to 75			
5	Divided injections, total 600 cc. in jugular	34	5.1	38	90	95		
8	Has drunk 475 cc. saline Heart 240; resp. 42				100	110		
12	Has drunk 525 cc saline	29	5.0	34	95	155	4500	8.4
18	Has drunk 770 cc. saline Heart 190; resp. 28; stood and walked, dragging hindlegs					220		
24	Has drunk 840 cc. saline Heart 220; resp. 30 alert	26	4.8	36	85	760		
36	Has drunk 360 cc. saline Blood in feces; weaker	32	5.2	33	70	260		
37	Injected 300 cc. saline in jugular; slightly improved				90	160		
40	Has had four injections in jugular, each 100 cc. saline Heart 260; resp. 40	23	3.2	29	65	90		
43	Divided injections—total 200 cc. saline in jugular Death by apnea Autopsy: veins full; intense engorgement of lungs	22	3.1	29	40	20	5270	9.1

dextran solution.[6] The fallacy behind plasma and all colloidal "plasma expanders" is shown in experiments with muscle trauma, burn shock,[3] and tourniquet shock,[6] where the strong tendency to hemoconcentration is not only overcome by plain saline but is converted into hydremic plethora. Smaller quantities of saline, which cause little or no plethora, give much shorter survival, and the aggravation of the congestion by colloids explains why the survivals are about half as long. These saline control experiments therefore represent the longest survivals obtainable with any treatment heretofore.

Can these results be improved by using alkali to correct the apparent acidosis represented by the reduced plasma bicarbonate percentage? To equate such disparate fluids as plasma and Hartmann solution implies a less accurate testing method than is supplied by severe shock in dogs. Therefore four dogs with five-hour tourniquet shock were given the recommended treatment, with Hartmann solution intravenously and a solution of 3.5 gm. of sodium chloride and 2.5 gm. of sodium citrate per liter administered by drinking or by stomach tube.

Table 2 illustrates the consistent results in all four animals; namely, increased edema, such as should be expected from alkali, and reduced survival, ranging from 21 to 28 hours.

Exploratory experiments were performed on six other dogs in similar shock; namely, two each with sodium lactate, sodium bicarbonate, and sodium citrate. All results corroborated the bad bicarbonate effects found by investigators from Cannon[21] onward. The various anions can be judged only by allowing for the benefits of sodium and water, which always prolong life in comparison with the survival of untreated animals. Hartmann solution is best because it is most similar to plain saline (only 0.31% sodium lactate in Ringer fluid). Stronger lactate, such as the customary M/6 solution, shortens survival. Sodium citrate by vein is hypotensive and toxic. In general, death is hastened by increasing the quantity of any alkali, and particularly by any plan of holding the plasma bicarbonate up to the supposedly normal concentration.

TABLE 2.—*Hartmann Solution by Vein and Citrate-Saline by Stomach for Five-Hour Tourniquet Shock in 15 Kg. Male Dog*

Time After Tourniquet Release, Hr.	Procedure Condition	Blood				Urine			
		Hematocrit, %	Plasma			Vol., Cc.	Sp. Gr.	Prot.	NaCl, Mg. Per 100 Cc.
			Prot., Gm. Per 100 Cc.	NaCl, Mg. Per 100 Cc.	CO_2, Vol. %				
Immediately After	400 cc. Hartmann sol. i. v. and 250 cc. citrate-saline by stomach tube Hindquarters displaced 4200 cc. water								
2	200 cc. Hartmann sol. i. v. once; "50 cc. cirtate-saline by tube three times Vomited 350 cc.	54	6.5	585					
3	200 cc. Hartmann sol. i. v. Weak; dyspneic; rapid hindleg swelling	65	5.7						
5	In divided doses, 700 cc. Hartmann sol. i. v.; 250 cc. citrate-saline by tube		4.7	608	38				
14	Has drunk 500 cc. citrate-saline; after blood samples, 200 cc. of Hartmann sol. i. v. Sits up feebly; hindquarters displace 6500 cc. water Urine alkaline		6.2			350	1.014	+	233
23	Drank large volume citrate-saline spilled remainder into urine; moribund	44	5.4	585	42				
26	Death Autopsy: intense lung congestion; huge edema from hindlegs to thorax					365 cc. urine with diarrheal feces			

TABLE 3.—*Hemorrhage and Sodium Bicarbonate Injections in 6.7 Kg. Male Dog*

Time, Hr.	Procedure; Condition	Blood: Hematocrit, %	Blood: Plasma Prot., Gm/100 Cc.	Blood: Plasma CO_2, Vol. %
0	Bled 75 cc.; moderate hyperpnea followed 25 cc. 4% sod. bicarb. i. v., drying, hyperpnea, struggle	40	7.2	49
½	Bled 75 cc.; increased hyperpnea 25 cc. 4% sod. bicarb. i. v.	33	6.7	42
¾	25 cc. Na bicarb. i. v.; refused water			
1	Bled 50 cc.; then 50 cc. plain saline i. v.	30	6.1	39
2	Bled 50 cc.; hyperpnea; 50 cc. 5% dextrose i. v.	34	5.7	41
3	75 cc. 5% dextrose i. v.; salivation			
3 ½	Bled 50 cc.; then 50 cc. 5% dextrose i. v.	29	5.5	38
4	Bled 30 cc.; 50 cc. 5% dextrose i. v.			
5	Bled 30 cc.; slow, very deep hyperpnea	26	4.9	37
6	Bled 30 cc.; 30 cc. 4% Na bicarb. i. v., salivation	31	5.3	37
6 ½	50 cc. 5% dextrose i. v., slight muscle tremors			
7	Bled 50 cc.; 50 cc. Na bicarb. i. v. Slow, deep hyperpnea; profuse, strongly alkaline saliva			
8	Bled 50 cc.; 50 cc. 2% Na bicarb. i. v. Slow, deep hyperpnea; profuse, strongly alkaline saliva; blood-streaked defecation			
8 ½	Bled 30 cc.; increasing muscle tremors	28	4.7	41
9 ¼	Unconcious; deep, audible hyperpnea; urine by bladder pressure 55 cc.; sp. gr. 1013, strongly alkaline, albumin negative, chloride trace Extreme muscle quivering			
9 ¾	Death by apnea; sample of heart blood Autopsy: lung edema; congestion of liver and intestine	28	4.6	36

One procedure would be to multiply such experiments so as to furnish formal proof of these points. It was preferred to revert to a large series of experiments which were performed in another connection in 1918 and could not then be published.[37] These observations on nonshocked animals reinforce and explain the results in shock and also throw light on the underlying concept of acidosis such as could not be gained from the shock experiments alone. Because the results were thus known in advance, it was possible immediately to perform six experiments of the type illustrated in Table 3.

The essential point in these experiments is that by successive bleedings to induce hy-

TABLE 4.—*Sodium Bicarbonate Intravenously in 12.3 Kg. Normal Female Dog*

Time, Hr.	Procedure; Condition	Blood: Hematocrit, %	Blood: CO_2, Vol. %	Blood Pressure, Mm.
0	After taking blood, injected 50 cc. 4% Na bicarb. i. v.; heart 80; resp. 16	43	51	130
½	Heart 90; resp. 12; salivated After taking blood, injected 50 cc. of 4% Na bicarb. i. v.	42	51	120
1	Heart 90; resp. 40; profusely salivated; depressed; refuses water	44	54	110
2	Very depressed; tremor of hindlegs; colon temp. 102 F; total 50 cc. saliva collected, strongly alkaline; no urine; refuses water; given 200 cc. water by stomach tube	43	51	95
3	Very depressed, apathetic, salivating; heart 84; resp. 28, hyperpneic; general tremor After taking blood, injected 100 cc. 5% dextrose i. v.	44	47	105
3 ½	Weak; lies flat; marked general tremor Injected 100 cc. 5% dextrose i. v.; no urine	42	48	100
3 ¾	Tremor; dangerous weakness and unconsciousness Injected i. v. 100 cc. isotonic saline with 2 cc. of 10% HCl; removed temporarily from table; hyperpnea; continued tremor and salivation			
4	Acid-saline injection repeated; tremor, salivation, and hyperpnea diminished			
4 ½	Heart 98; resp. 66, panting Urine 175 cc., pale, clear, sp. gr. 1.006; slightly alkaline; sugar and albumin negative; NaCl 210 mg. per 100 cc. Acid-saline injection repeated			
5	After taking blood, acid-saline injection repeated Hyperpnea and brief waking; tremor less; salivation stopped	42	38	90
5 ½	Heart 96; resp. 80, panting; colon temp. 104 F By stomach tube given 100 cc. saline with 2 cc. 10% HCl Dog wakes and walks feebly; urine 110 cc. very pale, sp. gr. 1.007, faintly alkaline; albumin negative; NaCl 166 mg. per 100 cc.			
6	Strong resistance to dose of 100 cc. saline with 2 cc. 10% HCl by stomach tube; very hyperpneic in struggle; walks better, but lies down; very depressed and weak	40	24	110

perpnea and the consequent respiratory "acidosis," followed by successive bicarbonate injections to raise the plasma bicarbonate toward the accepted normal level, animals can readily be made to die of alkalosis with normal or subnormal plasma bicarbonate concentrations. The lack of relation to the true guide, namely, the blood pH, is plainly shown by the strongly alkaline urine and saliva. The oliguria and isosthenuria also furnish a commentary on the supposed protection of the kidney by alkali, though abundant fluid (chiefly 5% dextrose) was given in the attempt to counteract any excessive concentration of alkali and to stimulate diuresis and favor the kidney function of preserving acid-base equilibrium.

Three other experiments illustrated the killing of normal dogs with alkalosis and tetany, without bleeding. The reason why or the mechanism whereby alkali induces hyperpnea is not clear, but in appearance the respiration surprisingly resembles Kussmaul breathing. Even here, properly regulated injections can bring about the fatal result with normal or only slightly elevated plasma bicarbonate levels. Table 4 is shown to illustrate a modification, with some additional instructive points.

In this experiment, two 50 cc. injections of 4% sodium bicarbonate solution one-half hour apart sufficed to cause alkalosis, not checked when the animal (not thirsty) was given 200 cc. of water by stomach tube and 200 cc. of 5% dextrose by vein. There was anuria, together with the typical profuse secretion of strongly alkaline saliva. The plasma bicarbonate varied only between 47 and 54 vol. %, and the practically unchanged hematocrit figures showed that blood dilution was not a factor. After three and a half hours the dog was prostrated, with general muscle tremors, though the blood pressure was not dangerously depressed. The control experiments showed that tetany continued beyond this point is irretrievably fatal. Therefore at this point neutralization of the alkalosis was undertaken by injections of hydrochloric acid in saline. The result was gradual subsidence of the tremor, the salivation, and (contrary to the traditional association of dyspnea and acidosis) the hyperpnea. The quantity of acid may have been unnecessarily large, for later the dog easily became hyperpneic when the plasma bicarbonate had fallen to 38 and 24 vol. %. Nevertheless, the urine at this time was still faintly alkaline. The previously administered sodium bicarbonate failed to preserve the so-called "alkaline reserve" of the blood plasma. Also, when the anuria of alkalosis had been changed to rather free diuresis by the acid, the sodium seemed not to be accounted for as bicarbonate in the faintly acid urine or as chloride. There remains the possibility of elimination through the alkaline saliva (perhaps also bile and pancreatic and intestinal juices) or of intracellular penetration accounting for the profound prostration.

The definite points in these findings are the fallacy of plasma bicarbonate as an indication of the base content of the body, and the early deaths of normal animals from moderate quantities of alkali as a commentary on the advocacy of large volumes of alkaline solutions for shock.

The suggestive findings in rats, together with the harmfulness of unbalanced sodium, reinforced theoretical reasons for testing the role of the neglected chlorine ion. For convenience, hydrochloric acid was used in the form of the official U. S. P. 10% solution.

Tourniquet Shock.—The dog in Table 5, with five-hour tourniquet shock, received hydrochloric acid in saline by vein and ammonium chloride along with the acid by stomach. Such animals in the first few hours show no greater benefit than with plain saline, but later the recovery is apparent. By the next morning this dog, instead of being in the usual progressive depression, was vigorous and eating.

In a series of five experiments, these results were more or less duplicated by administration of acid entirely by vein or entirely by stomach, except that with the

TABLE 5.—*Saline and Acid for Five-Hour Tourniquet Shock in 16 Kg. Female Dog*

Time	Procedure; Condition	Blood				Urine					
			Plasma								
		Hematocrit, %	Prot., Gm. per 100 Cc.	CO_2, Vol. %	NPN, Mg., per 100 Cc.	Vol. Cc.	Color	Reaction	Sp. Gr.	Prot.	NaCl Mg. per 100 Cc.
Before leg ligation	Hindquarters displace 6100 cc. water	35	6.6	42							
Before tourniquet release		44	7.2	36	38						
After tourniquet release, hr.											
1¾	In divided doses, 2 cc. 10% HCl in 400 cc. saline by vein; 3 cc. 10% HCl and 3 gm. ammonium chloride in 600 cc. saline by stomach tube										
2	100 cc. saline i. v.; remains weak, stuporous					70	Red	Acid	1.024	++	333
4	In divided doses, 200 cc. saline i. v.; 1 cc. 10% HCl and 1 gm. ammonium chloride in 400 cc. saline by tube					150	Less red	Acid	1.006	++	303
5	Dog sitting up; drank 400 cc. saline in 1 hr.	28	4.9	26	46						
6	Strong, alert; drank 1400 cc. saline in 1 hr.					320	Straw	Acid	1.010	+	561
19	Well except for paraplegia; eats; hindquarters displace 6850 cc. water	36	5.2	44	42	2359	Pale	Neutral	1.006	+	545
48	Well except paraplegia; hindquarters displace 5600 cc. water					Polyuria	Pale	Neutral	1.013	—	639

single route the recovery was slower. In three additional experiments, recovery resulted even when treatment was delayed for one or two hours after removal of the tourniquet. In longer delays without treatment, or delays of 13 or 31 hours under plain saline treatment, the animals failed to recover when acid was given but survived

TABLE 6.—*Acid for Five-Hour Tourniquet Shock in 6 Kg. Male Dog*

Time	Procedure; Condition	Blood			
			Plasma		
		Hematocrit, %	Prot., Gm. per 100 Cc.	CO_2, Vol. %	Blood Pressure, Mm.
Before tourniquet removal	Hindquarters displace 1050 cc.	41	6.5	33	90
After tourniquet removal					
5 min.	Injected 50 cc. 5% dextrose with 1 cc. 10% HCl i. v.; by stomach tube 100 cc. water with 1 cc. 10% HCl and 1 gm. ammonium chloride				65
¾ to 1¼ hr.	Three such i. v. injections and 2 such stomach doses, spaced				45
	Blood sample at 1¼ hr.; urine 55 cc. very pale, clear, sp. gr. 1.025, sugar and albumin neg.; unconscious, very weak	40		18	to 35
1½ to 3 hr.	Two injections, each 50 cc. plain 5% dextrose				
	Heart 136 to 240; resp. 20, hyperpneic; urine 25 cc., pale, clear, faintly acid; sugar and albumin neg.; unconscious, very weak				
3½ hr.	Evidently near death; blood dark, obtained slowly; hindquarters displace 1625 cc.				
	After taking blood, injected i. v. 100 cc. isotonic saline, then 100 cc. 2% NaCl	35	4.4	17	25
4 to 4¾ hr.	Three spaced injections, each 50 cc. 2% NaCl				70
	Partly conscious; heart 180, resp. 22; moderate hyperpnea				60
					80
5½ hr.	Trifle of acid saline i. v. caused acute apnea and impending death; restored by i. v. injection of 50 cc. of isotonic saline	38		16	50
5¾ to 7 hr.	Three injections, each 50 cc. of isotonic saline				60
	Urine 30 cc., water-pale, faintly acid; albumin neg.; unconscious, very weak; heart 180; resp. 12, deep and blowing				50
7½ hr.	After taking blood (dark color), injected i.v. 50 cc. 4% Na bicarbonate	37	4.2	14	70
8 hr.	Injected i. v. 50 cc. isotonic saline				60
	Hindquarters displace 2300 cc.				35
9 hr.	Taking blood sample (dark) precipitated death				
	Urine 35 cc., water-pale, neutral; albumin neg.; NaCl 66 mg. per 100 cc. Autopsy: lungs normal; liver congested; kidneys wet; intestine normal externally, contents bloody in duodenum, more so in ileum, no blood in colon; other viscera neg.	32		24	

unusually long. Post mortem, the malodorous fluid of the edematous legs and the blood and tissues of the congested lungs were found swarming with bacteria, showing the deaths were due to septicemia.

Table 6 represents a single experiment to test the effect of acid without sodium. The early collapse of strength and consciousness after only three and one-half hours is reminiscent of the effects of 5% dextrose or of dextran solution without sodium.[6] Also, the blood pressure fell so sharply that the period of severe hypotension must have intensified the shock. An attempt was then made to save the dying animal by injections first of isotonic saline and then of 2% NaCl, to correct the hypothetical dilution of sodium. The blood pressure was thus raised to 70 and 80 mm., but it could not be sustained by later injections of isotonic saline or sodium bicarbonate. Death occurred within the short time of nine hours. Of incidental interest was the failure of acid to prevent leg edema. The increase of volume of the hindquarters from 1050 to 1625 cc. during three and one-half hours of acid injections must have withdrawn considerable sodium from the blood, and the volume is comparable with the further increase to 2300 cc. during the ensuing four and one-half hours of sodium injections. The freedom of the urine from blood or protein was also remarkable.

Hemorrhagic Shock.—Three controls were used for the milder method of Wiggers et al.,[9] namely, bleeding the dog under local procaine anesthesia so as to maintain arterial pressure of 40-45 mm. for one and one-half hours. Three others were prepared with the complete Wiggers procedure, in which the above-mentioned hypotension period is followed by more bleeding to keep the pressure at 30-35 mm. for a final half-hour. The only open question was whether such animals might be saved by the large volumes of saline which were used for tourniquet shock, and which previous workers have not tried. Also, the alkalinity of some previously used fluids was objectionable. In hemorrhagic shock there is not the edema or the great thirst of tourniquet or burn shock. Large quantities of fluid given by stomach tube are usually vomited; therefore administration must be chiefly by vein. The few experiments showed that no amount of saline can save these animals, and the most extreme volumes are detrimental. The deaths occur as usual by apnea, with excessive volume and dilution of blood and pulmonary engorgement. Otherwise, the large series

TABLE 7.—*Acid-Saline for Hemorrhagic Shock in 14 Kg. Female Dog*

Time, Hr.	Procedure; Condition	Blood			Urine				
		Hematocrit, %	Plasma						
			Prot., Gm. per 100 Cc.	CO_2, Vol. %	Vol., Cc.	Sp. Gr.	Reaction	Prot.	NaCl, Mg. per 100 Cc.
0	Blood pressure 110 mm.	42	6.3	38					
0 to ½	Graded bleedings, total 490 cc., reducing pressure to 40 mm.								
½ to 2	Pressure kept 40 to 45 mm.	37	5.7	24					
2 ½	Finished reinjecting all blood; pressure 85 mm.								
3 to 3 ¾	Three injections, each 50 cc. saline with 0.5 cc. 10% HCl i. v.								
4 ¼	Injection repeated; pressure 110 mm.; appears comfortable; drinks 50 cc. saline								
4 ¾ to 5 ¾	Three injections as before; pressure 110-120 mm.; comfortable; drinks 50 cc. saline				260	1.008	Faint alk.	—	251
6 ¼	Injection as before (completing 500 cc. saline and 5 cc. 10% HCl); pressure 110 mm.; venous pressure increased								
7	Weak; drinks 40 cc. milk; urine smoky	34	6.0	33	160	1.014	Faint alk.	+	366
8	Has drunk 250 cc. saline, containing 0.5 gm. ammonium chloride								
14	Much stronger; refuses water and saline; drinks milk				220	1.014		—	650

published by the Wiggers group have been accepted as controls establishing the fatal character of this type of shock.

The dog in Table 7 is illustrative of acid saline treatment of three animals prepared by the above-mentioned milder method, namely, hypotension of 40-45 mm. for 30 minutes. In this instance the very gradual withdrawal and reinjection of blood actually lengthened the hypotension somewhat. The treatment was entirely with moderate amounts of hydrochloric acid in saline intravenously, except for the 0.5 gm. of ammonium chloride by stomach at the eighth hour, which was probably superfluous. From the initial rather low level of 38 vol. %, the plasma bicarbonate showed the usual fall at the end of bleeding, but at the seventh hour, after five hours of acid injection, the plasma bicarbonate had risen in correspondence with the dog's general improvement, indicating a physiological control rather than a mere passive store of sodium. There was only slight blood dilution, according to hematocrit and plasma protein figures. The blood pressure remained high enough for liberal diuresis, but there was the isosthenuria which is typical of shock with ample fluid supply. The urine at five and one-half hours furnished one of the examples in this series of clear straw color and absence of blood or protein after 350 cc. of saline with 5.5 cc. of 10% HCl had been injected intravenously. The urine at the seventh hour, after 100 cc. more of the acid saline, was smoky with blood. The urine at the 14th hour, after protein had disappeared, had the red-amber color, along with low specific gravity, which is usual at that stage, indicating pigment from blood destruction. Here is also one of the examples of the unexplained alkalinity of urine. The main point was the steady clinical improvement, in such fashion that the dog drank a little milk at the 7th hour, drank milk freely at the 14th hour, and after 24 hours was eating and acting normally.

This cure by acid saline was characteristic of all three dogs with this form of shock, in contrast with the fatality with plain (or alkaline) saline.

The dog in Table 7 is illustrative of three experiments with acid saline after the full Wiggers preparation (with local procaine, bleeding from the femoral artery to keep the pressure at 40-45 mm. for 30 minutes, then at 30-35 mm. for 30 minutes). The blood was reinfused by stages, the very first injection raising the pressure above danger level. The retention of fluids by stomach was

TABLE 8.—*Acid Saline for Hemorrhagic Shock in 10 Kg. Female Dog*

Time, Hr.	Procedure; Condition	Blood			Urine				
		Hematocrit, %	Plasma						
			Prot., Gm. per 100 Cc.	CO_2 Vol. %	Vol., Cc.	Sp. Gr.	Reaction	Prot.	NaCl, Mg. per 100 Cc.
0 to ½	Arterial pressure 125 mm. Graded bleeding of 400 cc. reduced it to 40 mm.								
½ to 2	Additional bleeding reduced pressure to 30-35 mm.	44	8.8	38					
2½	Taking blood sample makes critical collapse; pressure 20 mm.; dyspnea	39	6.0	25					
3	Finished reinjecting blood Pressure 120-130 mm.								
3½ to 5¼	Spaced doses totaling 350 cc. saline and 5 cc. 10% HCl i. v.; also 200 cc. saline with 2 cc. 10% HCl and 1 gm. ammonium chloride by stomach tube								
6	100 cc. saline with 2 cc. 10% HCl i. v. Deep slow hyperpnea; pressure 100 mm.				55	1.006	Faint acid	—	216
7½	Drinks 20 cc. milk; pressure 100 mm.; mild hyperpnea; 100 cc. saline with 2 cc. 10% HCl i. v.								
9	Stronger; pressure 120 mm.; heart 84; resp. 14, deep; blood in urine	34	6.8	29	155	1.008	Faint alk.	+	433
16	Has drunk 225 cc. saline; acts well; eats meat		7.0	27	310	1.015		—	733

greater than in most animals of this type. Blood dilution was comparatively slight, according to hematocrit and plasma protein figures. The plasma bicarbonate was lowest at the end of bleeding, and after acid administration (total 550 cc. of saline with 9 cc. of 10% HCl by vein, 200 cc. of saline with 2 cc. of 10% HCl and 1 gm. of ammonium chloride by stomach) it rose as part of the general improvement of the dog. Meanwhile there was moderate but not distressed dyspnea. The urine at the sixth hour was faintly acid and at the ninth hour faintly alkaline to litmus, with the usual low specific gravity, thus ruling out any large acid excretion or adjustment of acid-base balance by the kidneys. Proteinuria was brief, but the red-amber color was present, as previously noted.

The recovery of these animals appears deceptively easy in the mere figures. The actual clinical condition was often alarming, and the collapse was worse than in the previous three dogs with the milder preparation. It is possible that this record of uniform cure may be broken with larger numbers of animals or with slight variations of technique in different laboratories.

This possibility was illustrated in two experiments with a still severer preparation, namely, bleeding to hold the pressure at 40-45 mm. for 30 minutes and then at 30-35 mm. for 60 minutes. These animals died after 13 and 16 hours, respectively, and the attempt to match the greater severity of shock with greater acid dosage merely gave the shorter survival. It may be significant that the plasma bicarbonate, instead of rising, as in the animals that recovered, continued falling to levels as low as 16 and 12 vol. %. A physiological mechanism in regulation of blood alkali again seems evident. Urine was scanty and bloody. The highest acid doses produced severe, distressed dyspnea and evidently increased the pulmonary inflammation seen at autopsy.

Other observations, which need not be detailed, showed that if the withdrawn blood is not reinfused, acid saline cannot save life.

Comment

The experiments described above were summarized in a paper read before the American Physiological Society in New Orleans, Sept. 8, 1952. After the paper had been accepted for publication, I withdrew it for reasons stated in the next two paragraphs.

Causes of death.—The function of all organs necessarily suffers in shock, and our microscopic studies [12] confirmed the known fact of widespread congestive and degenerative changes in prolonged shock. The severer and more rapidly fatal the shock, the less severe are the morphological changes, down to the vanishing point. The immediate cause of death is vainly sought in adrenal changes (usually slight) or in liver congestion (often severe), partly because shock may kill more quickly than removal of either of these organs, and partly because the basic shock process is radically different from adrenal failure.[3] Wiggers demonstrated the important cardiac impairment, but it was early learned [21] that after death from untreated shock the heart could be revived to continue beating with perfusion. Both in untreated animals with oligemia and in fluid-treated animals with hypervolemia, impending death is averted by constantly more saline,[3,6] increasing the blood dilution and cardiac load still further; and when the limit is reached, death still occurs by apnea, while the heart continues beating strongly for some time. With this invariable apneic death there is pulmonary congestion, and it was interpreted as the ultimate failure of saline therapy in "irreversible" shock. Since untreated animals with the described form of tourniquet shock die within 1 to 6 hours, infection is excluded as a cause, and the same seems true when animals treated with alkali or a colloid (plasma or dextran) die within 12 hours. Since there is no external wound, the same assumption was made for the saline-treated animals surviving beyond 36 hours. But when microscopic studies became possible, they revealed swarming bacteria in the blood and tissues, especially of the

lungs, and smears and cultures showed many forms of cocci and bacilli.* Invasion from the intestine in the long agonal period is one possibility. Meanwhile antibiotics had become routine in the clinical treatment of shock patients, and some further experiments which I carried out, without laboratory control, indicated that the saline-treated dogs recover permanently if they receive antibiotics in proper time. In other words, the "toxic" factor in shock, which was evident in my experiments and in those of others is only infection,[41,42] and the position regarding saline treatment is stronger than was claimed, for, instead of merely lengthened survival, there is actual recovery, in contrast to the early deaths of animals treated with alkali or colloids. It is uncertain, and somewhat improbable, that infection is concerned in the hemorrhagic shock which Swingle called "irreversible."

Acidity.—The finding that saline-treated dogs can recover from supposedly hopeless shock with the aid of antibiotics led to a further consideration of the results with acid. Though it was found impossible to continue the desired experiments in order to settle such an important point as recommendation of acid in shock treatment, at least the existing observations are positive and unequivocal on the remarkable tolerance and relative harmlessness of acid, in contrast to the injuriousness of the commonly used alkaline solutions and the fatal effect of maintaining theoretically normal plasma bicarbonate percentages in severe shock. Further theoretical aspects may be discussed as follows.

Kidney Function.—Gross hematuria usually results from the abrupt administration of acid saline, being less severe when it is given by stomach than by vein. Everyday experience suggests that a mildly acid urine will not injure the kidneys. When there is debris of hemoglobin or other material to be dissolved out by alkali, this is a complication which must usually be dealt with after the acute shock crisis is past. Even with abrupt acid injections the hematuria is slight and represents mere irritation, not preventing as free diuresis as with administration of plain saline, and clearing up without residual lesions in all animals that recover. Aside from slow infusions of highly dilute acid, the instances in which ammonium chloride was given by stomach point to the preferred clinical method. Proteinuria is also the rule with any considerable administration of alkali, as illustrated with Hartmann solution in Table 2 and other mentioned experiments, but there is never gross hematuria. Isosthenuria is the rule with both acid and alkali in shock, or with plain saline, there being evidence of some diluting power, but never of concentrating power, until the shock subsides. Figures for nonprotein nitrogen in the blood with acid treatment do not exceed the elevation that is usual in shock. The profuse diuresis does not protect against acidosis in the manner that might be expected. Notwithstanding the fall of plasma bicarbonate, and the acid reaction which is expected in normal fasting animals, the reaction of the urine is only faintly acid, neutral, or sometimes slightly alkaline to litmus. A further anomaly was the strongly alkaline urine in some experiments with normal or subnormal plasma bicarbonate. The main lessons at present are the absence of real or lasting damage to the kidneys from reasonable acid administration during shock and the anuric influence of alkali, in contradiction to prevailing ideas.

Theory Concerning Alkali Therapy.—Since all the organic acids recommended for shock treatment are convertible into sodium bicarbonate, the present experiments are in agreement with the earlier condemnation of this compound, as well as with an unfavorable report on the succinate,[24] contrary to some former claims. The introduction of an analytical method for sodium bicarbonate was accompanied by a grandiose claim for it as the measure of an alleged "alkaline reserve" and a prognostic index in diabetic coma. It was universally acclaimed as an

* Miss Sara Scudder, chief bacteriologist at New York City Hospital, made the smears and cultures.

epochal discovery, without a single criticism that it was neither new nor true, and regardless of my objections from 1920 onward.[27,28,37] The same information had already been furnished by alveolar-air analyses, with no such exaggerated interpretation. The claim contravened elementary common knowledge, as follows: (*a*) It was unsound chemically, in attributing quantitative value to a mere percentage figure when the fluid volume was unknown but was known to be highly variable, thus assuming ability to measure the blood or body alkali in the oligemia of shock or diabetic coma, or in the same subject after rehydration, or in the huge cardiorenal edemas. (*b*) It was unsound physiologically, because the body is not a mere tank of sodium bicarbonate solution, and percentages of chloride or other electrolytes have never been taken as measuring the body content. Surprisingly, no physiologist ever questioned the observations[26] purporting to show that sodium bicarbonate is diffused uniformly through 700 cc. of fluid per kilogram of body weight, i. e., without regard to cell boundaries. (*c*) It was unsound clinically, because death in diabetic coma is due not to mere acid but to a specific intoxication; therefore the danger could not be measured even by a valid quantitation of alkali. Magnus-Levy,[44,45] by actual analyses, found 200 to 300 gm. of oxybutyric acid in the bodies of patients dying of coma, and Naunyn[46] calculated that neutralization would require 160 to 240 gm. of sodium bicarbonate. It has been suspected that such quantities of acid are produced only under the stimulus of alkali administration, but the bicarbonate dose supposedly requisite for neutralization would certainly be fatal. In 1948, again without evidence of therapeutic validity, the blood bicarbonate percentage was offered as an authoritative contribution to the shock problem,[18] particularly with reference to the assumed benefit of alkali for kidney function.

Theory Concerning Acid Therapy

1. Long ago, in his important observations on acapnia, Henderson[31] explained that when hyperpnea causes exaggerated expulsion of carbon dioxide from the blood, the neutrality which is indispensable to life can be preserved only by a migration of sodium from the blood plasma into the tissue cells. Accordingly, what is regularly called respiratory "acidosis" is actually a tissue alkalosis, the effect of which is seen when mere forced breathing brings on tetany and loss of consciousness.[31-36] This condition is exaggerated in the type of experiments shown here, in which the lowering of plasma bicarbonate by the hyperpnea of hemorrhage is combated by sodium bicarbonate injections, with the result of fatal alkalosis while the plasma bicarbonate is still normal or subnormal. Increased pulmonary ventilation is evident in severe traumatic shock. The intense hyperpnea of hemorrhagic shock comes on so rapidly that the fall of plasma bicarbonate could not be due to acid production and must represent migration of sodium. Yet the treatment for both these conditions includes administration of alkaline fluids on the basis of plasma bicarbonate percentages, a procedure which guarantees death in severe experimental shock.

2. The heavy morphine dosage necessary to stupefy cats and dogs creates anoxia, and presumably formation of acid suboxidation products, as in shock, but the narcotic reduction of CO_2 discharge makes a compensatory elevation of plasma bicarbonate.[39] On the other hand, the acid production in shock can scarcely compare with the production in diabetic acidosis at the same level of plasma bicarbonate. These comparisons strengthen the belief that the acid production in shock does not seriously overtax the body's neutralizing power, but that chiefly acapnia is accompanied by a tissue alkalosis, which may be relieved by acid, according to theory as well as experiments.

3. While an increased production of amino and keto acids is clearly a result of anoxic injury, particularly in the liver, it

may at the same time be an automatic part of the defense. The policy of one school of therapy is to oppose natural reactions. An example is the warming of shocked patients, defeating the natural tendency to a fall of temperature and metabolism, and thus increasing anoxia and mortality, whereas the opposite course, of assisting the natural process, reduces the need for oxygen and favors survival. Though death in shock is due specifically to anoxia, the reports of therapeutic administration of oxygen, by inhalation or intravascular infusion, indicate only trivial or doubtful benefit. My own unpublished results were negative with these methods, as well as with infusion into a portal tributary with a view to oxygenating the liver, and with a plastic tube passed from the carotid down into the abdominal aorta so as to administer oxygen directly to the injured legs. Since all other attempts at increasing oxygenation have been baffled, help may be found in acid, because it stimulates hyperpnea, and presumably the oxygen intake, and, furthermore, favors dissociation of oxyhemoglobin, with resulting release of oxygen to the tissues. Alkali opposes both these processes. Thus, insofar as acidosis exists in shock, its effect may be protective; and the further protection by acid and injury by alkali may be explained.

4. It has been necessary elsewhere [6] to dispel the strangely prevalent delusion that the danger in shock is oligemia and that colloid fluids are necessary to overcome it. Actually, in infusion treatments the danger is hypervolemia and pulmonary congestion, and it is easily shown in dogs that saline not only maintains full circulatory volume but also creates the least congestive danger. All kinds of infusions increase the edema of injured tissues. Physicians recognize alkali as favoring fluid retention and acid as favoring its elimination. It can be recalled that the observed diuretic effects in these experiments conformed to this law. Speculation is open on whether there may be a still deeper influence upon entrance of sodium and exit of potassium through cell membranes.

5. The alkaline reaction of the saliva, and occasionally of the urine, suggested that the plasma bicarbonate often does not correspond to pH shifts in the blood. According to the Root-Gregersen findings,[40] fixed base exceeds total anions in normal blood, and this preponderance is increased in shock. On the face of it this is a blood alkalosis, and the apparent acidosis was explained only on the pure assumption of the presence of an unknown acid. Such an acid might be conceived as a shock toxin, or as part of a defensive effort favoring release of oxygen. The replacement of an organic acid by a simple mineral acid may have physiological consequences, which in the present experiments have appeared to be beneficial.

Application to Diabetic Coma

Contrary to the original assumption of Walter and Stadelmann a century ago, diabetic coma is not a simple acid poisoning. Existing coma is not cured by alkali; and, though sodium bicarbonate was credited with deferring the onset for a brief period, it is now an interesting question whether sodium chloride might have been better. I [43] may have been first in noting, briefly, the resemblance of the terminal symptoms to those of shock. Kussmaul breathing appears precisely adapted to *Auspumpung* of carbon dioxide, and hence to respiratory "acidosis." Therefore, notwithstanding the undoubted acid production, the present experiments may for the first time suggest a possible rational foundation for Joslin's clinical contention of the harmfulness of sodium bicarbonate. Since anuria is one of the gravest complications of coma, the prevailing idea of acid injury of the kidney may be compared with the anuria with alkali and the diuresis with acid in shock experiments. There is at present no explanation of the great reduction of ketosis with certain kidney lesions [47-49] or of the imitation of Kussmaul breathing with alkali intoxication.

Remark

A recent paper [50] from the National Institutes of Health furnishes clinical con-

firmation of the fact that saline is fully as efficacious as plasma or other colloids in therapy of burn shock, but it also illustrates how alkalinity has become a routine feature of saline solutions in clinical and experimental use. It is noticeable that this practice is not supported by a single test demonstrating the benefit of alkali, but is a pure assumption, based chiefly on the concept that the plasma bicarbonate percentage is a measure of the sodium content of the body, which was a transparent absurdity from the outset. The fixity of ideas is such that a suggestion of preference for acid against alkali will arouse as much apprehension as was formerly aroused by reduced tissue temperature. The challenge to current ideas on reaction is so revolutionary in large fields of medicine and surgery that any investigator would desire positive support for such an isolated position. The obstacles blocking continuation of this research have proved insuperable, and after five years of delay there has remained only a choice between silence and a statement of deductions from limited experiments.

Summary and Conclusions

The confusion created by the considerable benefit of any sodium salt solution in shock necessitates using severe shock for accurate comparisons. The fatal effect of the customary alkaline solutions in severe hemorrhagic or traumatic shock is indicative of less obvious harm in milder shock and of the need to discontinue this clinical practice.

The assumption of the plasma bicarbonate percentage as the measure of a supposed "alkaline reserve," a concept which never had any scientific foundation, is disproved experimentally. Fatal alkalosis can exist with plasma bicarbonate concentrations within normal limits. On the other hand, the reduced plasma bicarbonate values in shock are misleading, since in dogs with severe hemorrhagic or tourniquet shock the maintenance of these values up to the theoretical normal level with the clinically recommended alkaline solutions guarantees death.

The present work is a rehabilitation of the chlorine ion, after the exclusive attention heretofore given to the beneficial sodium ion. Furthermore, while sodium without chlorine is harmful to the extent stated, theoretical and experimental evidence is suggested for the possible value of chlorine without sodium, namely, in hydrochloric acid. The fewness of experiments necessitates postponing a decision on the recommendation of acid in shock treatment. Even if the impression of benefit should be found erroneous, the excellent tolerance of considerable quantities of acid, in contrast to the harmfulness of alkali, in a condition universally classed as an acidosis is still a striking phenomenon. Sodium chloride and its components are specific in shock treatment, as against all other molecules or atoms. The ramifications of the problem in diabetes and other fields invite further investigation.

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Implantation of Plastics in the Breast

Complications in a Case

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Indications for increasing the size of "underdeveloped" human female breasts by the operation known as "breast plasty," which is described as the implantation of plastic sponges behind the breasts, are somewhat nebulously stated in the medical literature, but the procedure may be indicated for (1) the relief of psychic disturbances, actual or potential, presumably caused by possession of hypoplastic breasts; (2) the increase of breast mass for other reasons, e. g., social or economic, or (3) combinations of (1) and (2).

Most advocates of "breast plasty," writing in both the lay and the medical press, appear to claim relief of psychic disturbances as an indication for operating. Pangman and Wallace [1] reported upon 400 such implants in selected cases, some of which were apparently done for hypoplasia and others following mastectomy. They stated that their patients were uniformly pleased. In questionnaires sent to their patients, all but one replied that they would have the operation done if they had the choice again and that they would recommend it to their friends. Nearly all commented upon her greatly increased morale. Gillet [2] enthusiastically advocated the operation and illustrated several cases of excellent results, denying that serious complications occurred and stating that the prostheses were well tolerated.

Contraindications to this operation are likewise ill-defined and are not well substantiated by reports of complications or other difficulties, which would appear to include the following:

1. Immediate complications
   - (*a*) Infection
   - (*b*) Drainage
2. Late complications
   - (*a*) Possible carcinogenic properties of some plastic materials
   - (*b*) Increasing firmness of the plastic sponge with concomitant increasing dissimilarity to breast tissue
   - (*c*) Development of draining sinuses
   - (*d*) Disruption of breast function or appearance

Any of the above may necessitate further surgery.

Kiskadden [3] stated that considerable infection and drainage occurred with early attempts to increase breast mass by implanting plastics and that this necessitated the removal of many of the implants. Pangman and Wallace reported that when they were using plain polyvinyl formalinized (Ivalon) sponges as implants drainage developed after a large percentage of the operations and over 10% of the sponges had to be removed because of this. When they substituted compound sponges composed of an outer shell of spongy plastic and a water-impervious inner sponge, their results were more satisfactory.

The carcinogenic properties of plastics being implanted in humans are simply undetermined. To the best of my knowledge, no case of malignancy attributable to implanted plastics has yet been reported in humans. The first case of malignancy credited to plastic material embedded in animals appears to be that of Turner [4] (1941), who reported the development of sarcomas at the sites of implantation of Bakelite disks in rats.

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The Oppenheimers and Stout [5] made the chance observation that sarcomas developed around cellophane about two years after this material was used to wrap the kidneys of rats being used in hypertension experiments. This group of investigators [6,7] followed their observation with experiments to determine the carcinogenic properties of different plastics in various animals. Every one of 14 plastics tested proved to be carcinogenic in rodents, the incidence of malignancy varying from 4.5% to 45.4% with the plastic tested. The highest incidence occurred with cellophane B, that of Silastic (a silicone material) (40%) and of polyvinyl chloride (38.6%) following closely. Malignant tumors developed in 18.4% of the rats in which especially prepared and highly purified polyethylene (without plasticizer) was implanted.

In 1955 the Oppenheimer group [8] reported upon further experiments of this type. A wider variety of plastics, and also different forms of a given plastic, e. g., film, perforated film, and fabric, were embedded, and again malignant tumors formed around every kind of plastic tested, the only exceptions being a few instances in which no tumors were found around the fabric form of a plastic. The highest incidence of malignancy occurred with cellophane C film (46.1%). Implants of polyvinyl formalinized sponge resulted in three malignant tumors in 34 rats (8.8%); these tumors were found 567 to 857 days after implantation of the sponges. These investigators stated that the only property which all of the materials tested had in common was that of being a polymer.

Druckrey and Schmähl [9] also found development of sarcomas around polyethylene, polyamide, and polysterol polymers about 18 months after these substances were embedded intraperitoneally and subcutaneously in rats. They stated that these tumors metastasized and that the process was irreversible.

On the other hand, Schubert and Uhlmann [10] implanted synthetic polyamide materials intraperitoneally and subcutaneously in 211 healthy rats and found only 2 local sarcomas at the sites of implantation after 25 to 32 months. During the period of observation, several spontaneous benign and malignant tumors not associated with implants developed in their group of rats. They concluded that the occurrence of tumors around implants of plastics in rats is not significantly greater than the natural occurrence of tumors elsewhere and pointed out that the mesenchymal tissues of the rat frequently show spontaneous malignant changes.

Grindlay and Waugh [11] performed 37 experimental implantations of polyvinyl sponges in 28 dogs and found no malignancy around the sponges 2 to 18 months after implantation. They warned that long-term experiments must be conducted before polyvinyl sponge could be given unqualified approval for clinical use. Moore and Brown [12] conducted similar experiments with polyvinyl alcohol sponges in 50 mice and observed no malignancy developing over a 10-month period.

In the light of the experience of Turner, the Oppenheimer group, and Druckrey and Schmähl, it would seem that the periods of observation of Grindlay and Waugh and of Moore and Brown may have been somewhat too brief to warrant any definite conclusions regarding the carcinogenic potentialities of polyvinyl sponge. The Oppenheimers suggested that the 2-year period required for development of tumors in their rats might represent an equivalent of 10 to 15 years in humans.

The original thought and hope that plastic sponges implanted behind breasts would retain their resiliency and soft consistency, Kiskadden states, were based on wishful thinking. Experience has shown that spongy plastic material becomes impregnated with granulation and fibrous tissue and contracts to form a hard mass. Grindlay and Waugh found that polyvinyl sponges implanted in dogs developed a firmness approximating that of fibrous tissue and that the sponges

contained connective tissue and blood vessels. Moore and Brown observed that polyvinyl sponges became quite firm six months after they were implanted in mice. Pangman and Wallace reported that their early implanted simple sponges became firm to hard and that shrinkage of from 25% to 75% of the original volume of the sponge occurred; the degree of firmness was proportional to the degree of shrinkage.

Other complications which suggest that this operation may be ill-advised are illustrated in the following case report.

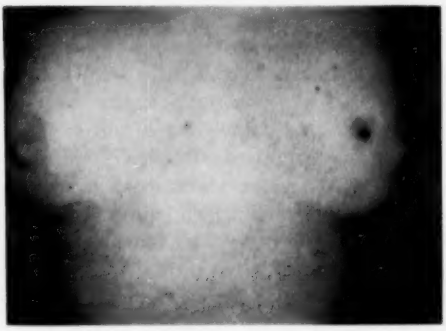

Fig. 1.—Preoperative photograph of breasts of patient, showing sinus opening in left breast.

Report of a Case *

History.—A 22-year-old white, married, nulligravid woman stated that she went to a doctor because of a "g-y-n condition." She stated that during his examination the doctor noted that her breasts were somewhat underdeveloped and "talked me into having them built up with plastic material." In June, 1954, plastic sponges were implanted behind each of her breasts. Except for a sensation of increasing heaviness and firmness in both breasts, she was pleased with the results of the operation until June, 1955, when a "red spot" appeared on the skin of her left breast. Two months later the "red spot" broke down and "pus" began to drain from the opening in the skin.

Examination.—The patient was a well-developed, well-nourished, young white woman who did not appear ill. There was a sinus opening about 1 cm. in diameter on the upper, inner quadrant of the left breast (Fig. 1). The opening was surrounded by a 1 cm. areola of thin, bluish-red skin. A thin, purulent material drained from the sinus opening, and this drainage could be greatly increased by squeezing the breast gently. Neither the lesion nor the breast was painful. Bits of material resembling bread crumbs could be extracted from the sinus tract in seemingly limitless quantities with a fine hemostat. Palpation revealed large, well-defined, biscuit-shaped, freely movable masses of firm, but somewhat resilient, consistency behind both breasts. The mass on the left appeared to be attached to the discolored skin around the sinus opening. Well-healed semicircular surgical scars were noted in both inferior pectomammary folds. No other physical abnormalities and no abnormal laboratory findings were noted.

Treatment.—Having no previous experience with similar cases, we resorted to the tenets of the basic surgical principle that no sinus containing a foreign body is likely to heal until the foreign body is removed.

On Aug. 31, 1955, the procedure of approaching the foreign body through the old operative incision, which seemed logical, was performed with the patient under general anesthesia. The plastic sponge was easily identified, well circumscribed in a mass of fibrous tissue (Fig. 2), and was freed from the surrounding tissue with ease by combined blunt and sharp dissection. At the discolored areola around the sinus opening, the skin was found to be attached directly to the sponge, and the sponge was devoid of fibrous tissue in this area. The wound was considered contaminated and was lined with dry, fine-mesh gauze and left unsutured. The wound appeared to be clean on Sept. 8, and, with the patient again under general anesthesia, it was carefully débrided and sutured. It healed uneventfully, and the patient was discharged from the hospital on Sept. 12, with instructions to return to the outpatient surgical clinic for removal of her sutures and follow-up observation.

Fig. 2.—Photograph of cross section of one of the prostheses removed from the breasts of the patient.

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Before being discharged, the patient requested that the remaining prosthesis be removed from her right breast. She gave the following reasons for this request: (1) She was "lopsided"; (2) she feared a complication in the right breast similar to that which had occurred in the left; (3) she desired and expected to become pregnant and feared some difficulty with the right breast if the prosthesis were left in place and she did become pregnant, and (4) mammary prominence no longer appealed to her vanity. It was deemed prudent to defer removal of the prosthesis from her right breast until it could be ascertained that her left breast was likely to remain healed and free from infection.

When she returned to the clinic, the wound in the left breast had remained clean and well healed. However, a discharge of serosanguineous fluid from the right nipple was discovered. This could be greatly increased by gentle pressure on the breast. She was readmitted to the hospital, and the prosthesis was removed from the right breast in precisely the same manner as that in which the one had been removed from the left breast. A sinus tract lined with gelatinous granulation tissue was found running from the depths of the plastic sponge through the natural breast to the nipple. She made an uneventful recovery from this second operation.

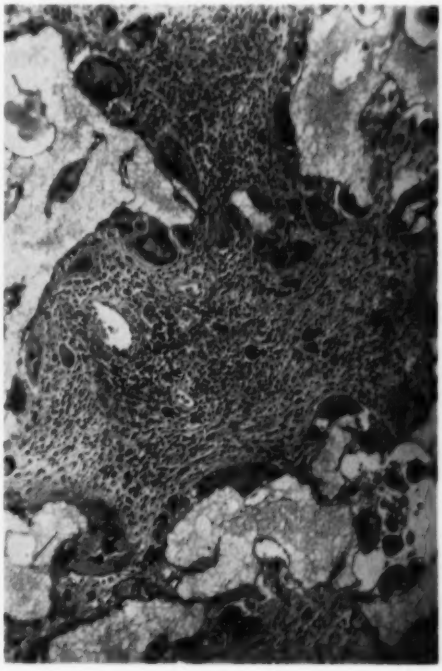
Pathology.—The specimens removed from the breasts were similar in pathologic details. The pathologist's interpretation of the specimen from the right breast is summarized as follows:

"Grossly, the specimen consisted of an ovoid mass, measuring 8.2×5.7×2.8 cm. The external surface was fibrous in nature and rough in appearance. Section revealed a spongy material of light color, resembling bread on cut surface. The spongy material was surrounded by a rim of granulomatous tissue, measuring approximately 0.7 cm. in thickness.

"Microscopically, sections of the tissue revealed a marked foreign-body reaction. The foreign body was trabecular in appearance, basophilic on staining and superficially, in certain areas, resembled a fungus growth. Surrounding these foreign bodies was a marked granulomatous reaction,

Fig. 3.—Photomicrograph at low magnification, showing the junction of the plastic sponge and the breast tissue. Marked infiltration of the plastic material by fibrous connective tissue and giant cells. The illusion gained from the gross specimen (Fig. 2) of a capsule around the plastic material is dispelled by noting that this capsule is actually an infiltration.

Fig. 4.—Photomicrograph at high magnification of section taken from the depth of the plastic implant, showing foreign-body reaction with numerous multinucleated giant cells of various sizes and a rather severe chronic inflammatory reaction with lymphocytes and plasma cells.



with diffuse infiltration by large and small foreign-body cells of the multinucleated type. The small margin of collagenous tissue surrounding the foreign body was also infiltrated with plasma cells, lymphocytes, and polymorphonuclear leukocytes. No evidence of malignancy was seen. A small amount of breast parenchyma was noted on the edge of the tissue" (Figs. 3 and 4).

Follow-Up Observation.—The patient has remained well and the wounds are well healed. At one of her follow-up visits she expressed vague anxieties, and possibly a guilt complex, over having had the plastic sponges implanted. One of these manifestations was in the form of an inquiry as to whether or not she was more likely to contract cancer of the breast for having had the plastic sponges implanted, a possibility which I had never suggested to her. The other outstanding inquiry was whether or not the original operation could have had any influence upon her apparent inability to become pregnant. She was reassured with negative answers to both these inquiries, the second with considerable more certainty than the first.

Comment

It is believed that this patient is suffering from vague anxieties and possible guilt complexes as the result of undergoing "breast plasty" and that these are at least equal in magnitude to any psychic disturbances which she may have suffered from "hypoplastic" breasts. She has undergone the considerable inconvenience and expense of two subsequent hospitalizations and four operations under general anesthesia as a direct result of the original operation. Her breasts are probably less attractive than before the "breast plasty." The possibility of increased hazard of malignancy and of difficulty in the events of pregnancy and lactation lies in the future. The person who performed the "breast plasty" is believed to be unaware of the complications which developed in his patient 12 to 15 months after the operation.

Summary

A partial review of the rather scanty professional literature regarding the implantation of plastic materials in underdeveloped human female breasts and some other mammalian tissues is conducted. Various opinions regarding the propriety of the operation known as "breast plasty" are reiterated. The problem of the potential carcinogenicity of plastic materials implanted in mammalian tissue is reviewed and discussed briefly. A case report illustrating certain late complications of "breast plasty" and the methods used in the management of these difficulties are presented.

Col. Howard A. Van Auken, Chief of the Laboratory Service, Fitzsimmons Army Hospital, Denver, furnished the photomicrographs, and Lieut. Charles E. Strickland (MC), U. S. Army, formerly Chief of the Laboratory, U. S. Army Hospital, Fort Hood, Texas, and personnel of the Fourth Army Area Laboratory, Fort Sam Houston, San Antonio, Texas, supplied the remaining photographs and made the pathological interpretation of the tissue.

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Studies on the Physiology of the Gastric Antrum

Effect of Antrum Resection on Secretion of Gastric Juice from the Isolated Stomach

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Recent studies from this laboratory, as well as elsewhere, have demonstrated that the antrum of the stomach is an important endocrine organ, distinct in function from other parts of the gastrointestinal tract. An understanding of the endocrine function of the antrum and of its external secretion should be helpful in the surgical treatment of peptic ulcer and provide a more complete understanding of the physiology of gastric secretion. In the total gastric pouch, the antrum is isolated from contact with food or distending stimuli and is continually bathed in the undiluted acid gastric secretion of the fundus. In a previous study from this laboratory it was concluded that in this situation the antrum is quiescent.[1] Removal of the antrum from the isolated stomach and its transplantation to the duodenum or to the transverse colon as a diverticulum caused a tremendous augmentation in gastric secretion. This stimulation in gastric secretion disappeared when the transplanted antrum was excised. In subsequent studies, however,[2] it was found that the application of acid to the antrum mucosa inhibited gastric secretion from the fundus. It was accordingly possible that the acid secretion in the isolated stomach coming in contact with the antrum mucosa might exert a continuing inhibition of secretion, and if this were true, removal of the antrum should result in an increase in acid output from the fundus. In addition to this possibility, it is known that the antrum mucosa secretes a mucilaginous, faintly alkaline secretion with considerable buffering capacity for hydrochloric acid. The significance of this neutralizing effect of the secretions of the gastric antrum has not been fully determined. For these reasons, the present experiments were devised to determine quantitatively the effect of excision of the gastric antrum on the secretion of gastric juice in the totally isolated stomach.

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Experimental Procedure

Healthy, adult mongrel dogs were used, and all operations were performed with the animal under general anesthesia and with the usual aseptic precautions. In the first group 15 dogs were prepared with totally isolated stomach pouches with vagus innervation preserved (Dragstedt pouch). In the second group, of three dogs, vagus-innervated total stomach pouches were prepared as before, but in addition the splanchnic nerve on both sides was excised. In the third group, of three dogs, isolated total stomach pouches without vagus innervation (Lim-Ivy type) were prepared. Quantitative collections of all gastric juice secreted by these isolated pouches were secured by means of stainless steel cannulae and rubber bladders, as previously described. After suitable control studies on the volume and acid concentration of the secretion from the intact pouches, the antrum was resected and the studies repeated. In addition to these 24-hour daily collections of gastric juice, in some cases the pouches were subjected to quantitative insulin and histamine tests both before and after the antrum was removed. The data from these latter tests will be discussed separately.

Results

1. *Effect of Antrum Resection on Daily Twenty-Four-Hour Secretion from a Vagus-Innervated Total Gastric Pouch.*—Total stomach pouches with intact vagus nerves were prepared in 15 dogs by the method of Dragstedt and Ellis.[3] Gastrointestinal continuity was reestablished by an esophagoduodenostomy. After recovery from the operation the presence of intact vagus innervation was established by a positive response to insulin hypoglycemia. The animals were fed a daily diet of horse meat, kennel mix, and 300 cc. of milk. Electrolyte balance was maintained by the addition of sodium chloride to the food. All of the animals in this series remained in good health and as a rule maintained their preoperative body weights. Quantitative 24-hour collections of gastric secretion were made in rubber football bladders attached to stainless steel gastric cannulae. The free acid was titrated using Topfer's reagent, and the results were expressed in clinical units. The hydrochloric acid output, in milliequivalents, was calculated by multiplying the volume, in liters, by the free acid, in clinical units. The results are expressed in milliequivalents of hydrochloric acid and percent of the control secretion of the intact pouch. After a control period of 4 to 11 weeks, the antrum was resected from the pouch. Great care was taken not to injure the vagus nerves at the time of surgery, and after recovery from the antrectomy preservation of the vagus nerves was verified by a positive insulin test. The secretory studies were then repeated.

It is difficult to define accurately the boundaries of the antrum in the living intact stomach, and especially difficult to determine the limits of the antrum in a previously constructed total gastric pouch. The weights of mucosa resected as antrum varied in this series from 7.2 to 22.4 gm., and the relative proportion of the antrum to the total amount of gastric mucosa varied from 10% to 19%. The total amount of gastric mucosa was determined by weighing the amount of mucosa remaining in the pouch when it was eventually removed. Thus it is quite possible that a varying amount of acid-secreting cells

TABLE 1.—*Effect of Antrum Resection on Mean Twenty-Four-Hour Daily Secretion from an Innervated Total Gastric Pouch*

		No. of Collections	Volume, Cc.	Free HCl, Cl. U.	HCl, mEq.	Per Cent of Control Secretion
D962	Intact total pouch	30	473	98	46	100
	Antrectomized pouch	30	404	105	42	91
D301	Intact total pouch	30	338	98	33	100
	Antrectomized pouch	36	232	91	21	64
D304	Intact total pouch	28	290	117	34	100
	Antrectomized pouch	30	138	107	15	44
D315	Intact total pouch	35	359	74	27	100
	Antrectomized pouch	102	456	95	43	159
D416	Intact total pouch	29	401	104	41	100
	Antrectomized pouch	30	253	119	30	73
D425	Intact total pouch	30	257	104	27	100
	Antrectomized pouch	30	189	103	19	70
D626	Intact total pouch	36	500	111	56	100
	Antrectomized pouch	37	563	116	65	116
D630	Intact total pouch	61	718	115	83	100
	Antrectomized pouch	49	710	119	84	101
D647	Intact total pouch	36	500	111	56	100
	Antrectomized pouch	37	563	116	65	116
D648	Intact total pouch	30	316	103	33	100
	Antrectomized pouch	43	249	94	23	70
D650	Intact total pouch	29	268	103	28	100
	Antrectomized pouch	47	271	116	32	114
D764	Intact total pouch	65	402	106	44	100
	Antrectomized pouch	50	325	115	39	89
D785	Intact total pouch	70	735	113	84	100
	Antrectomized pouch	40	883	117	105	125
D786	Intact total pouch	78	443	104	46	100
	Antrectomized pouch	45	371	106	39	85
D840	Intact total pouch	70	755	135	101	100
	Antrectomized pouch	15	467	119	55	54

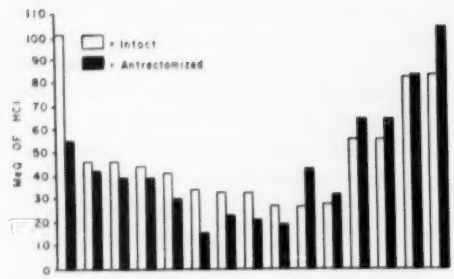

Fig. 1.—Effect of antrum resection on the mean 24-hour daily secretion from an innervated total gastric pouch (15 dogs).

may have been removed at this operation. This problem was minimized in several of the dogs by marking the estimated limits of the antrum with black silk sutures at the original operation.

The data are summarized in Table 1. In 9 of the 15 dogs the hydrochloric acid output decreased from 9% to 56% of the control secretion. Each of these dogs exhibited a decrease in the volume of gastric juice produced. In five animals there was a decrease in the concentration of free acid, while in four there was either no change or a slight increase. In the remaining six dogs there was an actual increase in the amount of hydrochloric acid, varying from 1% to 59% of the control level. In all of these animals there was an increase in the concentration of free hydrochloric acid. Five dogs displayed a concomitant increase in the volume of gastric juice, while in one there was a slight decrease in volume.

Whether the acid output rose or fell was mainly a reflection of the volume. Thus the average change in volume in the dogs showing a decrease in acid production was −28%, while the free-acid-concentration change was −0.7%. To a less extent this was true in those six dogs showing an increase in acid secretion. These data are summarized graphically in Figure 1. Statistical analysis of these data using the *"t"* test reveals that there is no significant difference in the milliequivalents of HCl output before and after antrum resection.

2. *Effect of Antrum Resection on Daily Twenty-Four-Hour Secretion from a Vagus-Innervated Total Gastric Pouch in Sympathectomized Dogs.*—In three animals the sympathetic nerves on both sides from Th6 down to include the splanchnic nerves were previously divided. Vagus-innervated total gastric pouches were prepared in these animals, and they were studied in the same fashion as that described above. Excision of the antrum resulted in a slight fall in both the volume and the free-acid output. The data are summarized in Table 2. Again, the differences shown are not statistically significant.

3. *Effect of Antrum Resection on Daily Twenty-Four-Hour Secretion from a Vagus-Denervated Total Gastric Pouch.*—In three dogs total gastric pouches were prepared as above except that the vagus nerves to the stomach were divided. After excision of the antrum there was no change in volume or total-acid output in one dog, a slight increase in one, and a slight decrease in the third. These changes are not statistically significant. The data are summarized in Table 3.

4. *Effect of Antrum Resection on Secretory Response of a Vagus-Innervated Total Gastric Pouch to Insulin Hypoglycemia.*—In these experiments the animals were fasted for 24 hours and were then given a

TABLE 2.—*Effect of Antrum Resection on Mean Twenty-Four-Hour Daily Secretion from a Vagus-Innervated Sympathectomized Total Gastric Pouch*

		No. of Collections	Volume, Cc.	Free HCl, Cl. U.	HCl, mEq.	Per Cent of Control Secretion
D189	Intact total pouch	24	488	101	49	100
	Antrectomized pouch	39	433	92	40	82
D235	Intact total pouch	47	408	118	48	100
	Antrectomized pouch	20	338	111	38	79
D273	Intact total pouch	36	630	134	85	100
	Antrectomized pouch	31	509	124	63	74

TABLE 3.—*Effect of Antrum Resection on Mean Twenty-Four-Hour Daily Secretion from a Vagus-Denervated Total Gastric Pouch (Ivy Pouch)*

		No. of Collections	Volume, Cc.	Free HCl, Cl. U.	HCl, mEq.	Per Cent of Control Secretion
D934	Intacy Ivy pouch	50	155	61	9.1	100
	Antrectomized Ivy pouch	50	149	61	9.1	100
D941	Intact Ivy pouch	40	212	54	11.7	100
	Antrectomized Ivy pouch	40	145	65	9.7	83
D967	Intact Ivy pouch	40	263	65	16.8	100
	Antrectomized Ivy pouch	110	261	84	22.2	132

TABLE 4.—*Effect of Antrum Resection on Mean Response of a Total Innervated Gastric Pouch to a Quantitative Insulin Test*

		No. of Tests	Volume, Cc.	Free Acid, Cl. U.	HCl, mEq.	Per Cent of Control Secretion
D315	Intact total pouch	5	68	108	7.4	100
	Antrectomized pouch	5	50	99	5.0	88
D416	Intact total pouch	2	27	48	1.30	100
	Antrectomized pouch	2	22	75	1.63	125
D626	Intact total pouch	2	44	89	4.2	100
	Antrectomized pouch	2	56	102	5.9	140
D630	Intact total pouch	2	60	89	5.9	100
	Antrectomized pouch	2	88	118	10.2	173
D647	Intact total pouch	2	50	110	5.6	100
	Antrectomized pouch	2	26	81	2.0	36
D648	Intact total pouch	2	52	71	3.7	100
	Antrectomized pouch	2	34	86	3.0	71
D650	Intact total pouch	2	52	115	6.0	100
	Antrectomized pouch	2	26	90	2.3	38
D764	Intact total pouch	2	28	72	2.2	100
	Antrectomized pouch	3	31	115	3.6	164
D785	Intact total pouch	3	89	110	9.8	100
	Antrectomized pouch	2	88	125	10.6	109
D840	Intact total pouch	2	50	109	5.5	100
	Antrectomized pouch	1	33	71	2.3	42

dose of 10 units of regular insulin intravenously. The gastric secretion was collected for 100 minutes. Usually the control secretion contained little or no free acid. These results of the tests are summarized in Table 4 and graphed in Figure 2. In 5 of the 10 animals there was an increase of up to 73% in the secretory response to insulin hypoglycemia after removal of the antrum, and in 5 animals there was a decrease of up to 64% after antrectomy. There was great variation in the individual responses both in volume and in free-acid output in all the dogs, both before and after antrectomy, and statistical evaluation with the "*t*" test showed no significant difference.

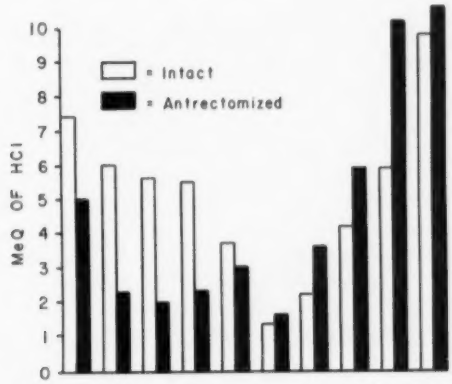

Fig. 2.—Effect of antrum resection on the mean response of a total innervated gastric pouch to a quantitative insulin test (10 dogs).

5. *Effect of Antrum Resection on Secretory Response of a Vagus-Innervated Total Gastric Pouch to Histamine.*—Histamine is a potent and consistent stimulus of the parietal cells. Standardization of the stimulus and collection period in each dog provided another possible method of evaluating quantitatively the secretory ability of the pouch before and after removal of the antrum. Histamine was given subcutaneously and the gastric secretion collected for a period of two hours. After removal of the antrum the same dose of histamine was re-

TABLE 5.—*Effect of Antrum Resection on Mean Response of a Total Innervated Gastric Pouch to a Quantitative Histamine Test*

		No. of Tests	Dose Mg.	Volume, Cc.	Free Acid, Cl. U.	HCl, mEq.	Percent of Control Secretion
D425	Intact total pouch	2	0.2	36	122	4.35	100
	Antrectomized pouch	1	0.2	48	105	5.0	115
D626	Intact total pouch	2	1.0	258	137	36.0	100
	Antrectomized pouch	1	1.0	292	139	41.0	114
D630	Intact total pouch	2	1.0	129	126	16.3	100
	Antrectomized pouch	2	1.0	144	130	18.6	114
D647	Intact total pouch	3	1.0	186	142	26.4	100
	Antrectomized pouch	1	1.0	208	129	26.8	101
D648	Intact total pouch	3	1.0	135	133	14.5	100
	Antrectomized pouch	1	1.0	144	129	18.6	128
D650	Intact total pouch	2	1.0	72	126	8.95	100
	Antrectomized pouch	1	1.0	102	131	13.3	149
D764	Intact total pouch	3	0.55	116	130	15.1	100
	Antrectomized pouch	3	0.55	116	142	16.6	110
D785	Intact total pouch	3	0.55	240	136	33.1	100
	Antrectomized pouch	1	0.55	144	130	18.7	56 *
D840	Intact total pouch	3	0.55	74	117	8.9	100
	Antrectomized pouch	3	0.55	134	122	16.3	183

* Bled from pouch on day before this test.

peated. The results are expressed in milliequivalents and in percent of the control response. These responses were assumed to measure the maximum secretory effort ("secretory mass") of the pouch. There was very little variation in these tests in the same animals. The data are summarized in Table 5 and summarized graphically in Figure 3. Eight of the nine dogs displayed an increase in acid output of from 1% to 83% after removal of the antrum. The decreased response shown by the one dog (D785) is probably not significant, since this test was done the day after the dog bled from the pouch. It is significant that in seven of the eight dogs the increase was due to an increase in volume. The free-acid concentration changed very little and actually decreased in three of the eight dogs. If the data are statistically analyzed after omitting those for D785, the increase in secretion is significant at the 5% level.

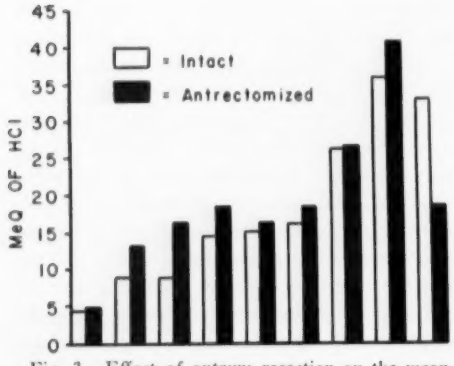

Fig. 3.—Effect of antrum resection on the mean response of a total innervated gastric pouch to a quantitative histamine test.

Comment

It has been demonstrated repeatedly that the gastric antrum can function in locations other than its natural one and that food is not essential for antrum stimulation. It would thus not be surprising if resection of the antrum from a vagus-innervated total gastric pouch produced an alteration in the secretory pattern.

On the basis of present information, three distinct contributions to the behavior of such an innervated total pouch might be ascribed to the antrum. In the first place, a thick mucoid material of excellent buffering capacity is secreted by the antrum mucosa. Elimination of this mucus would tend to decrease the volume of gastric juice but increase its acid concentration. An increase in acidity was observed in the 24-hour collections of gastric juice in 10 of the 15 dogs.

In 1942 Uvnäs [4] presented experimental evidence indicating that extirpation of the pyloric portion of the stomach or interference with its function by cocainizing the

mucosa or decreasing its blood supply resulted in a diminution of the cephalic phase of secretion. Previous studies from this laboratory [5] have demonstrated that removal of the antrum does not abolish the gastric secretory response to vagus stimulation, and this finding is confirmed in the present experiment. It is also clear that vagal innervation is not required for the release of gastrin. Nevertheless, there is considerable evidence supporting the position of Uvnäs indicating an interrelationship between the vagal and antrum phases of secretion. These data will be reported later.

Finally, the possibility of an inhibitory role of the antrum must be considered. Those stimuli which are usually sufficient to produce antrum function and gastrin release are ineffective if the pH of the antrum environment is in the range of 1 to 2.[2] In some way acid in contact with the antrum mucosa inhibits the release of gastrin. Recently evidence has been presented suggesting that under certain circumstances, namely, when it is bathed in an acid medium, the antrum elaborates a hormone which exerts an inhibitory effect on gastric secretion.[6] When one considers the possible role of the antrum in the total pouch, it is readily apparent that the circumstances necessary for the production of an inhibitory substance might well be present. Hence, removal of the antrum would allow the pouch to escape from this inhibiting influence.

The data from the sympathectomized dogs and the vagus-denervated pouches show slight changes following antrum resection. In the three sympathectomized dogs a slight decrease in secretion was observed. In the three vagus-denervated total pouches there was no change in secretion following antrectomy in one dog, a slight increase in the second, and a slight decrease in the third. These data throw little added light on the problem of the effect of antrum resection on total gastric pouch secretion other than to minimize the importance of vagus innervation.

Removal of the antrum resulted in an increased secretory response to histamine stimulation in practically all of the experiments. This is not easy to explain, since removal of the antrum had such a variable effect on the spontaneous secretion of the pouch. It is conceivable that the strongly acid environment resulting from histamine stimulation produced greater antrum inhibition than would be elicited by the less copious spontaneous secretion. Such an effect could be explained by the release of an inhibitory substance from the antrum mucosa on contact with acid.

Summary

Quantitative 24-hour collections of gastric juice were made in dogs with vagus-innervated total gastric pouches (Dragstedt type), in sympathectomized dogs with similar total gastric pouches, and in vagus-denervated total pouches (Lim-Ivy type) before and after removal of the antrum. Antrum resection produced inconsistent changes in secretion.

The effect of removal of the antrum on the response of the vagus-innervated total gastric pouch to a quantitative insulin test was studied. The change in response was unpredictable.

The secretory response of the vagus-innervated total gastric pouch to a standard dose of histamine was markedly increased after resection of the antrum.

The University of Chicago, 950 East 59th St (10) (Dr. Dragstedt).

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Open Heart Surgery

Introduction

A participant in a panel discussion is likely to feel less inhibited than is the author of a formal paper. In this respect, the panel discussion here to be reported was successful. It brought forth offhand declarations concerning policy, decision, and technic in open-heart surgery. It brought forth, also, the viewpoints of both internist and surgeon, and these viewpoints were not always the same. In addition, proponents, on the one hand, of extracorporeal circulation and, on the other hand, of hypothermia, spoke freely. Two leading advocates of extracorporeal circulation, moreover, were at variance on several matters.

Such free exchange gave to the listeners clearer understanding than they had had of the views expressed. Their perspective was improved. Finally, because great change in the field under consideration has not taken place since the discussions were held, the clarifications achieved will help toward solving problems of the immediate future.

Papers presented before the 1956 meeting of the International Society of Angiology appeared in the January and February issues of this journal. Unfortunately, the material presented by the panelists in their discussions at the same meeting was not made available for publication until a much later time. However, because of the value of the information, the Secretary of the Society and I consider publication advisable even at this late date.

WALTMAN WALTERS, M.D.

DR. TRAVIS WINSOR, Chairman, Los Angeles: Let us come to order, please. I should like to start by introducing the Moderator, who, in turn, will introduce the panel—Dr. Wilfred G. Bigelow, from Toronto, Canada.

DR. WILFRED G. BIGELOW: Thank you, Mr. Chairman.

To my far right, Dr. John W. Kirklin, from the Mayo Clinic, Rochester, Minn.; seated next to him is Dr. C. Walton Lillehei, from the University of Minnesota, and next to him is Dr. S. Gilbert Blount Jr., from Denver.

Open-heart surgery! This is the Cinderella of cardiac surgery. For the last 16 or 17 years, stimulated by the imagination of Dr. Gibbon, many university centers in this country have been working on the problem of extracorporeal circulation as a means of doing open-heart surgery.

Four or five years ago hypothermia loomed on the horizon as a threat to the heart-lung pump, and we found that with our present knowledge the time we could work in the heart was limited to from five to six minutes.

Very recently, from the University of Minnesota, and from the Mayo Clinic, we have heard of remarkable successes with the use of extracorporeal circulation. I think these reports are very important. They presuppose replacing standard operations with a new technique still in the stage of development.

Most of you in the audience have heard the panelists or read their papers, and I think you would like the opportunity to question them and find out what are the indications and the limitations of these two techniques of open-heart surgery; for that reason we will rely principally on your questions, which I would urge you to bring forward. I shall start right out with the first question which has come up here:

"What is the experience with open-heart surgery for aortic stenosis?"

Do you care to say anything in answer to that, Dr. Kirklin?

Submitted for publication March 5, 1957.

Panel discussion on Cardiac Surgery held at the Fourth Scientific Meeting of the North American Chapter of the International Society of Angiology, in Chicago, June 9, 1956. The other presentations at this meeting were published in the January and February, 1957, issues of the ARCHIVES.

DR. JOHN W. KIRKLIN, Rochester, Minn.: Yes, I should be delighted to. We have had no experience at all with that.

DR. BIGELOW: Do you think you should be interested in it?

DR. KIRKLIN: Yes, I am sure we should. The only question that comes to mind is what open technique one would wish to employ. It seems they are basically three. One is hypothermia; one is extracorporeal circulation with cardiac asystole, and the third is extracorporeal circulation with retrograde perfusion of the coronary arteries.

Certainly I am reasonably satisfied in my own mind that closed operations for aortic stenosis, whether congenital or acquired, have been, by and large, not as satisfactory as most other intracardiac procedures; so I feel we should do those open.

I think hypothermia is probably better, but this is all theory; we have had no experience yet.

DR. BIGELOW: Dr. Lillehei?

DR. C. WALTON LILLEHEI, Minneapolis: At the University Heart Hospital I believe we are convinced of the benefits of visualizing the operative field directly and are currently pursuing two methods of dealing with aortic stenosis by direct vision. Utilizing hypothermia, Dr. Lewis has performed three operations, one resulting in death. Of these three cases, one was congenital and two were acquired. The death was in an acquired case.

Utilizing the pump oxygenator with the patients at normal temperature, we have also performed three operations—all three patients had acquired aortic stenosis—the ages ranging from 28 to 59 years, with one death. The ability to work upon the left side of the heart by a perfusion technique has been greatly facilitated by the simple expedient of maintaining the heart by the retroperfusion of a mere trickle of oxygenated blood through the coronary sinus. The heart and lungs are totally by-passed, using the pump oxygenator, in the usual manner, and through this separate retrograde perfusion of a small amount of blood into the coronary sinus the myocardium is kept a nice pink color, the heart continues to beat in regular fashion, and thus one is allowed to open the ascending aorta with more or less impunity and to deal in somewhat leisurely fashion with defects of the aorta valve or of the coronary arteries themselves.

At operation we can see the issue of some desaturated blood from the coronary orifices, indicating the heart is being effectively perfused, as one can judge from its regular beat and oxygenated, pink myocardium.

Actually, for about 10 months during 1955 there were no aortic stenosis operations done at the University of Minnesota, although patients needing corrective surgery were presented to us and we have a fairly aggressive surgical clinic. The reason was dissatisfaction with our accomplishments in this condition with the closed method; so from January to October of 1955 nothing was done clinically while work was pursued in the experimental laboratory in these two directions, namely, hypothermia and the use of pump oxygenators for aortic valve surgery under direct vision.

DR. BIGELOW: Dr. Blount, can you add anything, or do you disagree with any of these statements?

DR. S. GILBERT BLOUNT JR., Denver: No. In Colorado we have operated upon five patients with aortic valve disease employing the technique of hypothermia with a direct vision approach to the aortic valve. In these five cases there have been no deaths—one was acquired and four were congenital. Of the four congenital cases, three were valvular and one subvalvular.

Being a cardiologist, and not a surgeon, I am particularly interested in the diagnosis and proper selection of candidates for the procedure. Certainly, most of these patients are seen in their late 50's and 60's, when the majority have markedly calcified and deformed valves; although it is my opinion that the open approach is the better one, I feel the results from such an approach will

reveal but slight improvement in a valve that is markedly calcified.

One patient was a woman 29 years of age with no evidence of calcification, and she had a fibrous valve that opened very nicely. All the other cases were congenital, and without calcification, and were amenable to valvuloplasty.

Of course, the great fear in the beginning was that air would pass down the coronary arterial system. However, it is fascinating to note, as the aorta is wide open and the coronary orifices are before you, a slight movement of the interphase between the air and the blood, but there is no forward progression whatsoever and air embolism has not been a problem in any case.

It is our opinion, given a valve that is reasonably pliable and not markedly calcified, that the open approach is certainly the method of choice.

DR. BIGELOW: Can I sum up the opinion of this panel by indicating that experience with calcified acquired aortic stenosis is very limited?

DR. LILLEHEI: All three of our patients had heavily calcified aortic valves, clearly visible in the ordinary chest roentgenograms.

DR. BIGELOW: You were happy about what you could do locally?

DR. LILLEHEI: The reason the patients were selected for the open approach was that they were in serious difficulty clinically and their aortic valves were heavily calcified. The results of the closed operations have been particularly unsatisfactory in patients with heavily calcified valves; so if one feels that the open technique is better, as I view it, one ought to select the worst patients for testing the open methods, since it is those patients who are most urgently in need of better treatment.

DR. BIGELOW: Well, Dr. Blount thinks we should select the best cases, without calcification, and Dr. Lillehei thinks we should select the worst; and that probably is about the present status of the open-heart approach to aortic stenosis. Obviously, the latter is being stimulated by the fact that there is a considerable mortality rate in the use of the closed technique and the results often leave something to be desired.

Now, we are getting quite a number of questions. May I ask the panel to shorten their answers so that we may answer as many as possible?

The next question reads:

"How do Drs. Kirklin and Lillehei feel at present about the 'induced-arrest' techniques with the pump oxygenators for open-heart procedures?"

Could you answer that, Dr. Kirklin?

DR. KIRKLIN: We have had no experience with induced cardiac arrest for open cardiotomy. We have had considerable experience in the laboratory. If one wishes to stop the heart for very brief periods of time, say 10 minutes, the problems are at a minimum; the heart starts, or, rather, restarts, readily, and the problems seem very few.

If one stops the heart for a 40-minute period, the problems become very considerable, as regards both getting complete and permanent arrest and restarting the heart.

The approach has obvious appeal. However, its main disadvantage seems to us at the moment to be that it robs one of knowing when a stitch may have caused heart block, and thus should be removed.

DR. BIGELOW: Dr. Lillehei?

DR. LILLEHEI: Dr. Kirklin has summed it up very well. Some of us older cardiac surgeons seem to be getting conservative. However, the chief value would be for left-side lesions, and one has an alternative method—retrograde perfusion of the coronary sinus. My feeling of preference for that method is related to the fact that in the seriously and desperately ill patient, who I think most needs this type of surgery, if one stops the heart, one is creating a metabolic oxygen debt within the myocardium that may well tip the balance against the patient, however expeditiously the corrective surgical procedure may be carried out.

DR. BIGELOW: Dr. Blount?

DR. BLOUNT: Our experience is entirely limited to the laboratory at present.

DR. BIGELOW: The next question reads:

"What is the lowest safe oxygen saturation with use of extracorporeal circulation?"

Dr. Kirklin?

DR. KIRKLIN: I don't know of any data on which to base an answer to that question. Our own experience has been limited to a technique in which we have 100% saturation of arterial blood at all times; yet, certainly, people live and walk around at a low arterial saturation. I don't know the answer to that question.

DR. BIGELOW: Dr. Lillehei?

DR. LILLEHEI: One has to take into consideration the flow rate and venous saturation. I see no reason not to have maximum physiological levels. In our own group of oxygenator cases the detailed physiological data from the first 80 have been analyzed recently, and the mean value for arterial blood (taken near the end of the perfusion) oxygen saturation was 96%.

DR. BIGELOW: Is everybody in agreement? The next question reads:

"What is the level of 'safe' hypothermia for repair of interauricular defect or pulmonary stenosis?"

Dr. Blount is considered a physician, but he works so intimately with the surgeons that he can move in and discuss these technical problems at a moment's notice.

DR. BLOUNT: That is a dubious distinction. Thank you, anyway.

We have recently—that is, in the past two months—altered some of our concepts relative to this very problem. In going over our first 111 cases, and on evaluating the mortality and morbidity resulting from hypothermia, we found that almost all complications of hypothermia were in patients whose temperature had been reduced to below 28 C (82.4 F).

As you know, the two main complications that we encountered were defects in coagulation, either thrombosis or hemorrhage, and the development of ventricular arrhythmias. However, those patients that were not taken below 28 C presented no such complications. Thus, at the present time, we do not take any patients below 28 C. Of course, this restricts the uses of hypothermia by limiting the time in which one has to work within the heart; therefore, with patients having complicated lesions we feel definitely that hypothermia is a method that should not be employed.

In patients with pulmonary stenosis and having intact ventricular septa, where the defect can be handled within a period of from two to three minutes, the temperatures are reduced to 31.5 C (88.7 F), and there have been no complications in 25 patients and no deaths. Patients with atrial septal defects have their temperatures reduced to the range of 29 to 30 C (84 to 86 F).

If, when the right auricle is opened, the surgeon considers that the defect is a simple one and that it can be closed within a period of five minutes, then there is no problem. If there are anomalous pulmonary veins or if, for other reasons, the closure presents technical difficulties, he works for four minutes, then closes the right auricle, reinstitutes circulation for a period of 15 minutes, and then reopens the auricle for a second period of work on the defect.

With employment of this technique there have been no difficulties whatsoever with the previously noted complications; therefore, I should say that at present we do not reduce the temperature below 28.5 C (83.3 F) and do not consider that a period of occlusion should be longer than six minutes at one time.

DR. BIGELOW: Thank you, Dr. Blount.

It is interesting to note that most of us using hypothermia have arrived at pretty much the same conclusion. Animal work would indicate that it is perfectly safe in the region of 24 to 25 C (75 to 77 F), but I think we have all found that clinically it is not safe below 28 C. I don't know what happens. There are interesting biochemical and electrical studies which would indicate that something happens below 28 C. There

is danger from increased myocardial irritability and a bleeding tendency. So it seems that the temperature should be from 28 to 31 (82.4 to 87.8 F), at the upper end of that range for pulmonary stenosis and at the lower end for other defects.

Would you like to comment, Dr. Lillehei?

DR. LILLEHEI: Dr. Lewis feels very much the same. In other words, they are using lower degrees of hypothermia as time goes on.

DR. BIGELOW: The next question reads: *"Dr. Blount, you have published data on hypothermia arrhythmias. Considering this complication, what is the optimum temperature for surgical procedures?"*

Dr. Blount, you have more or less answered that. Arrhythmias seem to appear at temperatures below 28 C. A temperature of 30 C appears to be a good safe one. There is a great deal of difference as regards age, and, of course, the younger children or infants can tolerate lower temperatures.

Here is a very technical question: *"1. Discuss filters in relation to pump oxygenators.*

2. Discuss bubble traps in relation to pump oxygenators.

3. Are filters useful in removing bubbles?"

Dr. Lillehei?

DR. LILLEHEI: We generally use filters. I know some are not using them. We have done one operation recently without them, and it seemed to be perfectly satisfactory. However, I don't think proper filters cause any difficulties, and they are certainly a safeguard to the patient. And it is a source of comfort to the surgeon to know that if clots get into the system they will be extracted.

DR. BIGELOW: Dr. Kirklin?

DR. KIRKLIN: We use a filter. It doesn't have very much in it at the end of the operation except for a few specks of fibrin, but we do use a filter.

DR. BIGELOW: Another part of that question concerns the advantages. You have mentioned them already.

Here is a question in a different vein: *"Do you think that a ruptured aortic sinus can be repaired?"*

Dr. Blount?

DR. BLOUNT: Yes, I think such a defect can be repaired, and has been reported. We have not had the opportunity to operate upon such a defect, but I feel definitely that it could be repaired.

We have had the opportunity of repairing one aortic septal defect with the use of hypothermia when the entrance was from the pulmonary artery. I think that a rupture of an aortic sinus could probably be approached in the same way from the aorta.

DR. LILLEHEI: We have had experience with one patient, a 10-year-old girl, who was referred to us by Dr. Dennis, of New York. She had had an exploration in 1952 for a possible patent ductus. She did not have a patent ductus. Her arterial pulse pressure was 100/0, by oscillation. She had a severe growth deficit, weighing only 34 lb. (15.4 kg.) at 11 years of age. We used the pump oxygenator, with cross clamping of the aorta just below the takeoff of the innominate artery. The coronary sinus was perfused in a retrograde manner to support the myocardium, as mentioned above in regard to aortic stenosis. The fistula was into the right ventricle. Reparative surgery in this dry field under direct vision presented no difficulties, and she convalesced without difficulty, has gone home, and is continuing to do well.

DR. BIGELOW: Dr. Kirklin?

DR. KIRKLIN: I have nothing on that.

DR. BIGELOW: Here is a question that I perhaps should have brought out when we were discussing cooling.

"For interatrial septal defect, what is the most desirable open technique?"

Would you give your somewhat biased or unbiased opinion on that, Dr. Blount?

DR. BLOUNT: There are probably at least five techniques by which an interatrial septal defect can be closed quite adequately, and I am sure that one's feelings are molded a great deal by one's personal experience.

I certainly feel that hypothermia affords a safe and adequate method for closing an atrial septal defect.

I think that in the case of the so-called ostium secundum, or uncomplicated, defect the extracorporeal circulation or pump oxygenator will not replace the technique of hypothermia for closing the defect.

Certainly, in the more complicated cases, in which there is no rim of tissue above the valve cushions, and the auriculoventricular valves are involved, and thus a longer time will be taken for the repair, the extracorporeal circulation-pump oxygenator method is desirable.

In the uncomplicated type, in our experience, the safest and best way is the method of hypothermia.

DR. BIGELOW: Dr. Lillehei, would you care to address any remarks to this subject?

DR. LILLEHEI: I believe that all atrial defects requiring correction should be closed by open techniques. There are a number of reasons for this, which may be summed up succinctly—the results are better. The percentage of patients with only partial closure of their defects is high with closed methods. Even though they may survive, this can hardly be considered a satisfactory result. Of open methods, hypothermia has given excellent results, but I personally prefer the pump oxygenator because of the added safety afforded by unlimited time and freedom from arrhythmias. Ostium primum is not satisfactorily handled by either closed methods or by hypothermia because of the conduction difficulties and the time required. A perfusion method at normal body temperature is essential for these defects.

DR. BIGELOW: Dr. Kirklin, what do you think about applying the rather complicated technique of extracorporeal circulation to relatively similar conditions?

DR. KIRKLIN: In the case of so-called ostium primum defect, I am in complete agreement with what has been said. I perhaps would say only one thing in mild disagreement. I think the words "open-heart surgery" have come to be a sort of slogan, and I am not sure it is justified. Certainly, some defects can be operated on in a number of ways, and there is adequate and incontrovertible evidence that it does not always have to be by open-heart surgery. I personally am not interested in jumping on a band wagon which says that all heart operations must be done with the heart open.

We follow pretty much the criteria already laid down; we continue to do the operations the way we have done them over the last three or four years. In those cases in which there is some suspicion of complications we use extracorporeal circulation. We have encountered three patients in whom we thought the defect would be complicated, and it turned out to be an ordinary atrial defect; the mortality has been zero in this very small group, and I am sure it will continue to be extraordinarily low. I do not think the fact that the method is safe necessarily means it should be used. I believe there are simpler ways.

DR. BIGELOW: Do you think neither of the open-heart techniques is really justified?

DR. KIRKLIN: I did not say that; I did not mean even to imply that, because I think Dr. Blount's and Dr. Lillehei's statements are entirely accurate; there are several good ways of doing the repair which carry very little risk, and I think the individual surgeon must be allowed some choice as to what technique to employ—and hypothermia is one of those ways.

DR. BIGELOW: You are not claiming any special advantage in your technique; you feel it can be done equally well with the other two techniques?

DR. KIRKLIN: We have continued to use the atrial well, which, in a way, I hesitate to say anything about, in this era of opening the heart and looking at everything. We have had experience with a number of cases. We have lost 3 patients out of 85, and 1 of those was a 12-year-old child with complicated conditions, and the other 2 were 45 and 48 years of age; so with a low

mortality and a high incidence of complete repair, I am not about to give it up.

DR. BIGELOW: You have not exactly answered by question, but I gather you feel that if a person can produce good results with whatever technique he uses, and with reasonable risk, that technique should be accepted?

DR. KIRKLIN: Absolutely. The criteria for any operation are low mortality and the ability to get the job done. Some repair atrial defects by straightforward closed techniques; others, such as Dr. Swan and Dr. Lewis, have accomplished the same results, with low mortality, through hypothermia, and I think one can accomplish it through the atrial well.

We are in a fortunate position in having several good techniques to choose from. They are all good enough, and I don't think we necessarily have to use the newest technique if the problem can be handled satisfactorily in other ways.

DR. BIGELOW: We do not mind your mentioning those closed techniques periodically during this panel discussion.

Could I ask a question? Have you had an opportunity to look at the Ivalon (polyvinyl formalinized) sponge at a rather late date?

DR. KIRKLIN: All three of the deaths we have had have been in the early postoperative period. The latest was on the sixth postoperative day. When Dr. Edwards initially opened the heart, it was difficult to see the sponge. It gets covered over rapidly with a layer of cells, and it looks very good at that point. We have seen it in a dog up to a year after operation, by which time it is completely covered over and the fibroblasts have grown into it and securely anchored it in place. We have not seen calcification in any of the sponges in the heart at three years by the ordinary roentgen technique. I feel that the evidence is good that the sponge is well tolerated and perfectly satisfactory.

DR. BIGELOW: Our particular group is using the hypothermia technique. There is a question reasonably closely related to this: *"With hypothermia can the right ventricle be opened for repair of infundibular stenosis with some degree of safety?"*

Dr. Blount?

DR. BLOUNT: Yes, it certainly can. In the group that comprises our total cases, we have operated in 15—I think the figure is correct—cases with infundibular stenosis, and in this number there have been 3 deaths.

Certainly, when one enters and operates upon the right ventricle under conditions of hypothermia, the tendency toward ventricular arrhythmias is higher than when one enters the right atrium. Without going into whether one should or not, in the case of tetralogies, to answer the question briefly, one can remove an infundibular stenosis under hypothermia with but moderate risk.

DR. BIGELOW: You will probably agree, Dr. Blount, that the essential difference between opening the pulmonary artery and opening the right ventricle is that, unless one has a very good clamp, one must have the circulation occluded during the operation, and probably for the closure of the right ventricle; so there is an added time factor which is very important.

As you know, if one opens the base of the pulmonary artery, one can put a clamp on it and reinstitute circulation and sew up the hole at leisure; but a defect in the ventricle may perhaps double the time.

DR. LILLEHEI: Another element that bears on this decision as to method is not whether one can do it, but whether it should be done in view of the patient's best interests. I refer to the problem of diagnosis. We have operated upon four patients with a preoperative diagnosis of isolated infundibular pulmonic stenosis with use of the pump oxygenator. Three of those four patients were found to have unsuspected ventricular defects in addition when the heart was open under direct vision. To be sure, these defects were ones that could be closed by two or three stitches, but under

hypothermia there would not have been sufficient time to deal with these additional defects. Many of us feel that when a patient's heart is operated upon, it is undoubtedly better to plan to do the complete correction at the initial operation. "Second looks" in cardiac surgery are difficult, dangerous, and inadvisable.

DR. BIGELOW: Do you think most of these patients have ventricular defects?

DR. LILLEHEI: Three of the four did, and possibly the first patient did, too, and we did not see it. If one does not look specifically for these ventricular defects, one is very likely to miss them.

DR. BIGELOW: Do you think, Dr. Blount, that we should relegate the infundibular stenosis group to a technique allowing us more time?

DR. BLOUNT: I would certainly agree with Dr. Lillehei that isolated infundibular stenosis must be rare, for we have certainly had a very similar experience. I think that it will come to that, yes. I think that in the future patients who have infundibular stenosis will be operated upon only by a method of extracorporeal circulation. Certainly, one hesitates to operate upon a tetralogy now by the direct approach and make no attempt to close the ventricular defect.

I remember suggesting to Sir Russell Brock that the reason he was obtaining such good results was that he was doing half the job. In other words, he had removed just enough of the infundibular stenosis that the flow was greatly increased, but not enough so that the stenosis was completely removed. In the case of large septal defects, complete removal of the pulmonary obstruction will result in sudden development of very significant left-to-right shunts, with great enlargement of the heart in the immediate postoperative course.

DR. BIGELOW: What did Dr. Brock say when you made that remark?

DR. BLOUNT: Well, we were in swimming at the time, and I ducked.

DR. KIRKLIN: I feel personally that infundibular stenosis should be operated upon with extracorporeal circulation, because in that disease the lesion is not adequately treated by the closed technique, and we must define as our goal the complete relief of the obstruction.

We have operated on seven patients with either pure infundibular stenosis or combined valvular and infundibular stenosis. We have been fortunate in losing only one of the seven, and that was from the development of multiple intestinal obstructions and complications three months after operation.

Infundibular stenosis can be adequately treated, and the gradient can be abolished, and I think one has immeasurably more safety inside the ventricle with extracorporeal circulation than with hypothermia.

DR. BIGELOW: I presume the patient would have to be in a reasonable state of debility before you did that, wouldn't he?

DR. KIRKLIN: I am not sure that I know what you mean. Perhaps to answer your question I should say that these patients have all had right ventricular pressures in excess of 140 mm. Hg. We have had enough experience to know that under circumstances such as these the risk is reasonably low—one death out of seven, and that in a 45-year-old woman, who, as I say, died three months later. I think that experience justifies going ahead in a situation where we know the future holds danger.

DR. LILLEHEI: In a patient with pulmonary infundibular or valvular stenosis, symptoms have not been a reliable guide for surgery. We generally base our indications upon right ventricular pressures, taking into account the patient's age. There are variations for different ages, but in general pressures above 75 or 80 mm. Hg would make the patient a candidate for corrective surgery.

DR. BIGELOW: This runs right along with the problem of pure pulmonary stenosis. Can we have some remarks on that, Dr. Kirklin?

DR. KIRKLIN: I think Dr. Blount should discuss pure pulmonary stenosis. I assume by your question, Dr. Bigelow, you are

speaking of a patient with no underlying infundibular stenosis?

DR. BIGELOW: Or with a small atrial septal defect.

DR. KIRKLIN: In our hands at the present time, if a patient with so-called isolated valvular stenosis is desaturated, we would use extracorporeal circulation, close the interatrial defect, and open the pulmonary valvular stenosis. The difficulty, it seems, in outlining in a didactic way the treatment for pure valvular stenosis without cyanosis is the uncertainty regarding underlying infundibular stenosis. If we have had a strong suggestion of underlying infundibular stenosis, then we have done the operation with extracorporeal circulation.

We have in the past continued to use the closed technique in cases not thought to have an infundibular stenosis or an atrial defect, although Dr. Blount has convinced me beyond a shadow of doubt that hypothermia and direct operation on the valve are profitable, and I am sure we will turn to that.

DR. BIGELOW: It seems to be the experience of most people interested. The initial suggestion, made, I think, before this Society by Dr. Henry Swan, that the original closed techniques have left a great deal to be desired has been pretty well accepted, wouldn't you think, Dr. Lillehei?

DR. LILLEHEI: I disagree to this extent. I think the Brock operation is fundamentally a good operation for isolated pulmonary valvular stenosis, and he and Mr. Sellers deserve a great deal of credit for originating and carrying it out. Its failures are most frequently related to applying the technique to patients with unsuspected associated defects, such as atrial septal defects, ventricular septal defects, atresias of the pulmonary outflow tract, and infundibular stenosis.

Mr. Brock and I have discussed this quite recently, and I believe he is quite in agreement with what I am about to say; namely, that the problems related to the closed method of pulmonary valvulotomy are the problems of accurate preoperative diagnosis. If your diagnostician can give you pure pulmonary valvular stenosis with a guarantee of freedom from any associated defects, which he cannot, of course, I think most experienced surgeons can do an excellent job with the Brock technique. The problem revolves around the patient with these associated defects. For those patients the surgeon needs additional reparative procedures, if he is going to cure them physiologically. Further, I wish to emphasize that with the open approach to the pulmonary valve from above, utilizing hypothermia, one is not in an appreciably better position to deal with these associated lesions than with the closed technique.

For that reason, more recently we have preferred an open approach in all patients with pulmonary valvular or infundibular stenosis, utilizing the pump oxygenator at normal temperature. The incision begins in the infundibulum and extends across the pulmonary annulus into the pulmonary artery. This technique permits an unhurried visualization of the whole right ventricular tract. If an unsuspected infundibular stenosis or ventricular septal defect is present, as happens, this defect can be dealt with before the annulus of the pulmonary valve is carefully reconstructed and the incision in the outflow tract of the right ventricle and pulmonary artery closed.

DR. BIGELOW: Dr. Lillehei, in your defense of the Brock-Sellers operation, what have you to say about the inability in some cases to obtain postoperative catheterization pressures in the right ventricle approaching normal after that operation?

DR. LILLEHEI: I think that in a reasonable percentage of the cases one gets satisfactory results. In addition to the above-mentioned reasons, a point worthy of mention is the surgeon's experience. In the first few cases done by any one operator, he often feels he was lucky to get the knife in and out without a mishap; but as he gains experience and confidence, he learns to dilate the valve vigorously after it has been cut with the knife.

There are some interesting experiments in our laboratory that indicate that experimentally produced pulmonary valvular stenosis results in an associated acquired infundibular stenosis, due to the right ventricular hypertrophy. It is a questionable and arguable point as to whether in man, when the valve is properly opened, that associated infundibular hypertrophy will regress by itself, and, if so, how long it will take. It is quite possible that this muscle should be resected at the same time to achieve a fully curative physiological result.

DR. BIGELOW: We are all waiting for your remarks, Dr. Blount.

DR. BLOUNT: We certainly feel that the direct approach to the valve from above under the conditions of hypothermia is the procedure of choice. Now, as regards the results prior to the advent of the open approach, seven patients were operated upon via the right ventricular approach, and certainly our results now are more satisfactory. The Brock approach resulted in a satisfactory reduction of the gradient in but one patient. However, of the 20 patients operated on by the open technique whom we have now recatheterized after surgery there has been a satisfactory reduction of the gradient in 17, that is, a gradient of less than 20 mm. Hg.

Two things have been of interest. In two or three patients the gradient has not been satisfactorily reduced, and there has been a residual gradient; the systolic pressure in the pulmonary artery would be on the order of 25 to 30 mm. Hg and that in the right ventricle, on two occasions, as high as 70 mm. Hg. This is now considered to be the result of the great hypertrophy of the structures in the outflow tract of the right ventricle.

One of these patients has been recatheterized a year after the first postoperative catheterization, and in this particular patient there has been a further drop in the systolic pressure within the right ventricle from 70 to 35 mm. Hg.

We have encountered two patients in whom the gradient has been completely removed, but pulmonary hypertension has developed, the systolic pressure being between 40 and 50 mm. Hg in the pulmonary artery.

We are recatheterizing these patients at yearly intervals for continued evaluation. However, it is our conviction that the open approach utilizing hypothermia is the procedure of choice in the treatment of pulmonary valvular stenosis with intact ventricular septum.

DR. BIGELOW: There are some interesting points here. Dr. Lillehei points out that continued high right ventricular pressure following a closed technique might be due to inadequate experience in the proper opening of the valve, or to the presence of unrecognized infundibular stenosis or septal defects; do I quote your correctly?

DR. LILLEHEI: Yes, sir.

DR. BIGELOW: When Dr. Swan cited these results, he did choose the surgeons who had the most experience. I think perhaps this question will be answered only when we have a long enough follow-up and enough cases treated by the open technique to determine the answer. If we can do a large enough series with the open technique, and know we have a *good* opening, and find that in the vast majority of those patients the pressure does fall to a normal range, we may suspect that the *poor* results in the closed technique are to a great extent due to an improper opening.

If I may move into this discussion for a moment, stimulated by this work of Dr. Blount and Dr. Swan, a study was made of cases at our Children's Hospital, and there was found to be a similar problem of persisting high pressure after what was considered adequate operation. We have used open techniques under hypothermia in a small series of 10 patients through a midsternal incision without entering the pleural cavity, and half of them have been recatheterized, with return to normal pressure. It is only a small group, and it is something

to which the panel will perhaps agree that we shall not know the answer for a while.

Dr. Lillehei, I believe, mentioned unrecognized infundibular defects; this problem probably resolves itself to a great extent into one of the excellence of our preoperative diagnoses.

Our roentgenologists feel they can usually detect in adults an infundibular stenosis, and determine what its size and position are; I would like to echo your remark and say that that probably is a key factor in determining the type of procedure to use.

Would you like to say something more about this, Dr. Lillehei?

DR. LILLEHEI: I should be very dubious about the radiologist's ability to tell accurately the presence and amount of infundibular stenosis for one simple reason; that is, in the open curative operation for tetralogy sometimes we have been deceived by our own eyes, with the right ventricular outflow tract wide open, as to how much infundibular stenosis was present. On several such occasions we have closed the heart, taken the patient off the pump-oxygenator, measured the pressures, and found that there was a substantial gradient left between the right ventricle and the pulmonary artery. Then, we have reopened the heart and found the location of the stenosis and removed it. If, then, it is a treacherous and deceptive matter even under direct vision, I remain unconvinced that a roentgenologist can tell anything accurately enough to guide the surgeon in this situation.

DR. BIGELOW: There are two questions here that I might take the liberty of answering, since we have had a prepanel discussion. I perhaps know how the panel feels about the open-heart treatment of aortic insufficiency and mitral insufficiency. I think I am right in saying that the panel does not think there is any particular place for open-heart surgery in those two conditions.

DR. LILLEHEI: I would not want to go on record as such. We have operated upon four patients with mitral or aortic insufficiency by open methods. Most of this experience has represented learning phases of technique and pathology. I am quite encouraged that something better can be accomplished by open methods, especially if the results are measured against the accomplishments of the closed techniques for these same lesions.

DR. BIGELOW: Do you think that this surgery, before it makes any great strides, will await the development of some prosthesis?

DR. LILLEHEI: I don't know. I think prostheses are something like Communism—you either believe in it or you don't. I don't believe in them.

DR. BIGELOW: I would like to ask the members of the panel how they feel about the place of these more complicated surgical techniques, extracorporeal circulation and hypothermia. Dr. Kirklin, do you think they are ready now for universal use?

DR. KIRKLIN: Well, I hope they are. We are using them; so we feel they are. Of course, one always gets in trouble in his own mind, and also in other people's minds, when he says that something is now completely worked out and ready for general use. I don't know how one ever arrives at such a decision. One can only evaluate his own experience and decide whether, in his hands, the technique seems to be satisfactory. Certainly, so far as extracorporeal circulation is concerned, we intend to use it on more and more occasions. We have abundant evidence now that the technique is satisfactory and that it can be applied with safety under proper circumstances.

That should not, however, be interpreted to mean that there are no problems connected with extracorporeal circulation. Those working with hypothermia have shown us beautifully that even a relatively simple technique has many problems. The problems are not mysterious; they are open to study and analysis, but they exist. I think the same is true of extracorporeal circulation; there isn't anything normal about it, and, being an abnormal state, it is accompanied by a number of problems. Those

problems are soluble and manageable, but they exist. I think everyone going into this work must be aware of these problems and must be willing to accept the difficulties encountered in solving them.

DR. BIGELOW: Do you have any philosophical comment to make, Dr. Lillehei?

DR. LILLEHEI: I think that open-heart surgery is a great new field of surgical endeavor. I know that some are sitting back on their hands waiting for the perfect method. There is no perfect method, and there is not likely to be. However, there will be a continuous improvement and refinement. There are almost a dozen methods for working inside the heart that have achieved some success.

The important result of that fact is that the emphasis has already shifted in many research centers in this country from work on methods for intracardiac surgery, per se, to work upon application of open-heart surgery to the many types of cardiac lesions likely to benefit from it. To date, at the University of Minnesota Heart Hospital we have operated upon 232 patients by open methods; yet it is a disturbing fact that at this date patients with intracardiac defects are being born locally at a rate far exceeding our capacities for repair—not to mention the acquired lesions or the backlogs of patients in need of this surgery elsewhere in the world.

DR. BIGELOW: Dr. Blount?

DR. BLOUNT: I have nothing to add.

DR. BIGELOW: Well, I think everyone agrees that this is a magnificent new era we are moving into, and probably a word of warning is in order. If one embarks in this field, one should have adequate research and clinical facilities to do this work and to do it properly.

I wish to thank the members of the panel, and to thank the audience for their participation and the many questions they have brought forth. (Applause)

Examinations for Certification in General Surgery

Last fall I was one of several guest examiners invited by the chairman of the American Board of Surgery to participate with members of the Board in giving Part II of their examinations for certification in General Surgery. The manner in which this oral examination was conducted and the results reviewed and discussed by all the examiners in general impressed me so much that I thought more surgeons should be informed about this examination. Each candidate had previously successfully passed the written Part I.

Guest examiners met with members of the Board on each of the two mornings that the examinations were given and were briefed by the chairman concerning the method of conducting the examination and its objectives; emphasis was placed on a kindly and understanding approach, without any queries about the site of the candidate's medical, intern, and residency or fellowship training. It was suggested that if the candidate did not appear to be too well informed on a certain subject, he be quizzed for a while on other subjects, with return to the first one later; an attempt then should be made to approach the subject from a different angle.

Each candidate was quizzed for an hour by two separate pairs of examiners, each team consisting of a member of the Board and a guest examiner. A patient was assigned for study, and a discussion was held with the first two examiners. After a short rest the second group of examiners took over and quizzed the candidate on different aspects of surgery, with occasional questions on recent advances and their contributors. In the afternoon examinations in anatomy and pathology were given.

The guest examiner could appraise the examination being conducted by the Board member and vice versa. An account was kept by each examiner of the candidate's answers, particularly those which showed a broad knowledge in the field of the question or a lack of it—this record was used at the end of the day, when all the examiners met and each candidate was evaluated. On the basis of 100, the grade of 75% was passing. If either group of examiners graded the candidate below passing, the reasons had to be given and recommendation made for or against a repeat oral examination without further training. If one team of examiners gave a good mark and the other a mark below passing, information as to where the candidate had his graduate training and the report of his work while taking it was read by the secretary of the Board, and his grades for the anatomy and pathology examinations were read. If they were above passing or better than the average, further discussion of the candidate occurred, and frequently his lower grade was increased, usually to passing.

Several of the candidates who passed with creditable marks had failed one part of the examination previously. In the group of about 70 who took the examinations, approximately 75% passed—a percentage which I am told is about the average for Part II of the examination.

The organization of the American Board of Surgery was completed in 1937. The Board was created in accordance with the action of the Advisory Board for Medical Specialties as approved by the Council on Medical Education and Hospitals of the American Medical Association. The various Boards have the twofold purpose of certifying those found to be qualified after meeting

reasonable requirements and of improving existing opportunities for the training of specialists within the field concerned. This is done for the protection of the public and the good of the specialty.

The cooperating surgical societies selected to form jointly the American Board of Surgery and the number of representatives appointed by each are as follows:

American Surgical Association	4
Section on Surgery of the A. M. A.	4
American College of Surgeons	4
Southern Surgical Association	1
Western Surgical Association	1
Pacific Coast Surgical Association	1
New England Surgical Society	1
Central Surgical Association	1
	17

The term of membership is for six years except when the Board shall elect members to shorter terms, which it may do at its discretion. Each cooperating association has power to appoint its representatives on the Board subject to the approval of the Board. No member of the Board is eligible for reappointment. Approximately 6000 surgeons have been certified in General Surgery to date.

WALTMAN WALTERS, M. D.

Surgical Residency Training in the United States Navy

World War II forcefully emphasized the imperative need for supplying expert surgical care for battle casualties as near the scenes of combat action and as soon after receipt of injuries as logistics and operational war conditions would permit. The Korean conflict merely served to add to the accentuation of and justification for this concept, with resultant refinements and advances in the techniques and speed of transporting battle casualties to surgical units where early definitive care could be provided for many, often within 20 to 30 minutes or an hour after they were wounded. As a consequence, considerable improvements were made over the outstanding records of World War II, when approximately 97% of all combat casualties reaching definitive surgical care stations survived. Additionally, the sharp reduction of morbidity, the early relief of human suffering, and the elevation of morale among thousands of the wounded were highly important factors not well reflected in statistical tables.

Within a year after cessation of hostilities of World War II, the Bureau of Medicine and Surgery of the Navy Department, fully realizing the urgent requirements of the Naval service for qualified specialists resulting from the rapid demobilization of large numbers of doctors with specialized training and anticipating a continuing and increasing need for an adequate number of these officers in the Medical Corps of the Regular Navy, undertook urgent measures in an attempt to remedy this desperate situation. Thus were established the first augmented and formalized residency training programs in surgery, as well as in other specialties, in the history of the Medical Department of the Navy.

The programs in surgery have been conducted in such a manner as to meet the accreditation requirements laid down by the Council on Medical Education and Hospitals of the American Medical Association, the American College of Surgeons, and the American Board of Surgery. Of particular helpfulness and essence in these endeavors are the great contributions of eminent civilian surgeons who had extended periods of active duty during World War II or acted in the capacity of consultants to the Surgeon General of the U. S. Navy during and since that War. These physicians gave unstintingly of their time, professional and organizational knowledge, and constructive guidance in the original founding of the surgical residency training programs in 1946. These extremely valuable and essential relationships and cooperation with the Bureau of Medicine and Surgery have continued up to the present time, represented by the Reserve Consultants and the groups of Honorary Consultants to the Surgeon General. In addition, it has always been the firm policy of the Bureau to maintain a close liaison with civilian educators and training activities and to obtain the services of a sufficient number of highly qualified civilian consultants to U. S. Naval Hospitals to meet not only training needs, but also the concomitant demands for improved standards

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The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

of medical care for military personnel in both teaching and nonteaching type hospitals. Their participation is vigorous, inspired, and realistic, involving, as it does, a close working rapport with a carefully selected and qualified surgical staff in each hospital. These civilian services represent a well-balanced distribution of effort, extending not only into the field of lectures, but, more importantly, into matters such as ward rounds, small group discussions of individual patient problems, analysis of history and physical examination findings, differential diagnostic procedures, instruction in the techniques of surgery by the performance of surgical operations, interpretation of special tests, advice on treatment plans for difficult or unusual conditions, and recommendations and assistance on matters relating to residency training practices.

The Navy offers in its own hospitals a total of 64 A. M. A.- and Board-approved residencies in Surgery. Residencies also are available in the surgical specialties of Orthopedic Surgery, Ophthalmology, Otolaryngology, Gynecology, Urology, and Thoracic Surgery. Residency training for medical officers is sponsored in selected civilian institutions for those surgical specialties wherein the Navy does not conduct Board-approved programs. These include Plastic Surgery, Neurological Surgery, and Children's Orthopedics, the last constituting one of the four years of total training for those who have completed or are about to complete three years of training in programs approved and accredited for Adult Orthopedics and Fractures.

Eligibility to compete for residency training under Naval auspices is, in the main, confined to medical officers of the Regular service. Medical officers of the U. S. Naval Reserve on active duty may be considered for residency training in Surgery or surgical specialties when shortage of supply of Regular trainees exists in those fields at the time applications for training are received. However, Reservists, to be eligible for consideration for such assignments, must have already completed all active military service obligations imposed by the Universal Military Training and Service Act, as amended. In return for each year of residency training received in a U. S. Naval Hospital, each medical officer is required to serve one year of active duty, exclusive of each residency year. The obligation for Navy-sponsored residency training in civilian institutions is two years for the first year of training and one year for each year of training thereafter. Thus, the obligation for a four-year surgical residency in a civilian institution would be five years, and in a U. S. Naval Hospital it would be four years.

During the past seven years 450 physicians have received part or all of their surgical residency training as medical officers of the U. S. Navy, mostly as Regulars in U. S. Naval Hospitals. Up to 18 months ago, all too many of these left the service for civilian life after completion of their obligated service for training received. But a steadily increasing trend has developed since that time, wherein medical officers who have completed their training are electing to remain in the Navy as Regulars, not only as a career for assignment to billets commensurate with their professional skills but as highly capable surgeons who contribute immeasurably to the perpetuation of the training programs in Surgery. On Jan. 1, 1957, there were 102 Board-certified or Board-eligible general surgeons on active duty, most of whom are medical officers of the Regular establishment. Current estimates indicate that in four years the number will have increased to about 165, which more nearly approaches the Navy's minimal peacetime operational requirements.

That the residency training programs furnish a major initial incentive for transfer to the regular Medical Corps of the U. S. Navy is evidenced by the fact that the majority of officers accepting such commissions during the past few years did so for the purpose of being assigned to those programs. Indications now point increasingly to the likelihood of a good majority of these men making a career for themselves in the Medical Department of the Navy. It will be a very happy and fortunate circumstance, indeed, if this pattern continues to prevail, for the so-called Doctors' Draft Law is just as unpopular with military authorities as with their civilian counterparts and with the profession of medicine at large in the United States. The only remedy for this difficult and trying situation is a potent nucleus of career medical officers. The Medical Department of the U. S. Navy, as well as of the U. S. Army and the U. S. Air Force, are urgently in need of the positive assistance and staunch support of all civilian physicians throughout the United States for the purpose of attracting a sufficient number of physicians to careers in military medicine to fulfill the critical responsibilities called for in our Constitution and in the Public Laws of the Congress. The potential catastrophic consequences of enemy thermonuclear, biological, and chemical warfare attack render it absolutely imperative that medical professional societies, organizations, institutions, and individuals everywhere in the country come forth with positive programs of action to help the Medical Departments of the U. S. Navy and her sister services accomplish their cardinal missions. The new Public Laws of the 84th Congress relating to military career incentives, dependent medical care, and survivors' benefits, including Social Security, all should attract more physicians to electing the military as a financially sustaining, professionally rewarding, and wholesome career.

Capt. Robert B. Brown
and
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Case Reports

Malignant Melanoma of the Anorectum

Report of a Case Without Recurrence Forty-Three Months Following Only Local Excision

JACOB G. PROBSTEIN, M.D., St. Louis

The anorectum is the third most frequent site of origin of malignant melanoma, following only the skin and eyes. Malignant melanotic tumors originating at this junction spread by direct extension, by lymphatic pathways, and via the blood stream. Accordingly, they have been treated by radical surgical intervention, which has usually included an abdominoperineal resection, followed in some instances by block dissection of ileoinguinal lymph nodes. Despite such drastic therapeutic measures, results have been uniformly poor, and survival for three years or longer has been unusual.

The case reported here is that of a patient who remains alive and well, without evidence of recurrence or metastasis, 43 months after therapy consisting only of a wide local excision.

Report of Case

The patient was a 65-year-old married white woman whose chief complaint on admission was of occasional episodes of rectal bleeding for six months. During the same period she had had intermittent diarrhea, constipation, and mucoid stools but had experienced no rectal pain or discomfort. There was no history of weight loss.

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Carl G. Moyer, M.D., Professor of Surgery, Washington University School of Medicine, gave advice during the study.

From the Department of Surgery, Washington University School of Medicine, and the Division of Surgery, the Jewish Hospital.

The past history was significant only in that she had had a vaginal hysterectomy 18 years before. Physical examination was negative except for rectal findings.

Rectal and proctological examinations revealed a firm, 2.5 cm. polypoid growth on the anterior wall of the rectum about 0.5 cm. above the anus; the mass showed no tendency to bleed on manipulation. There was no palpable lymphadenopathy.

A biopsy specimen of the lesion was taken by the referring physician and reported by Dr. Herman T. Blumenthal, of the department of pathology of the Jewish Hospital, as a malignant melanoma. Because of the generally poor prognosis with this lesion in this location, only a wide local excision was performed.

The pathological specimen consisted of three small pieces of polypoid tumor tissue, the smallest of which measured 6×4 mm. and the largest 22×10 mm. in diameters. The tissue had a deep reddish-black color. Two of the specimens were surrounded by a 1 cm. rim of normal mucosa. Microscopic sections showed both anal (Fig. 1) and rectal mucosa, beneath which there was a tumor composed of elongated fusiform cells, sometimes forming whorls. Distributed through these cells were somewhat larger cells, both fusiform and ovoid, which contained melanin (Fig. 2). There was no difference between the characteristics of the excised tumor and those of the previous biopsy specimen. The tumor extended to the surface, replacing in some sites the normal mucosa.

The postoperative course was uneventful, and the patient has now survived 43 months, without evidence of either local recurrence or metastasis.

Comment

Reports dealing with malignant melanoma of the anorectum have been published in recent years by Weston and Marren,[4] and by Delaney, Scudamore, and Waugh.[2] The latter authors point out that melanomas

Fig. 1.—Section shows surface squamous-cell epithelium of the anus adjacent to the ulcer. The submucosa and muscularis are replaced by a compact cellular arrangement of tumor cells. Black spots represent melanin deposits. Hematoxylin-eosin stain; mag. approx. × 100.

which involve mucous membranes carry, if possible, an even less favorable prognosis than those occurring elsewhere. There appear to be only slightly more than 100 cases of malignant melanotic tumors of the anorectum in the literature at present.

Because of this relatively small number of cases, evaluation of therapeutic measures is difficult. Delaney, Scudamore, and Waugh [2] have recently recommended resection of the abdominoperineal type with wide excision of the perineum and levator muscles, followed in four to six weeks by block dissection of the ileoinguinal lymph nodes.

Despite such radical therapy, local recurrence is frequent, and Bacon and Pena,[1] in reviewing the first 85 cases in the literature, reported that metastasis had been seen in every case regardless of therapeutic measures employed. In one-half the 10 cases comprising two reports from the Mayo Clinic death was from metastasis in seven

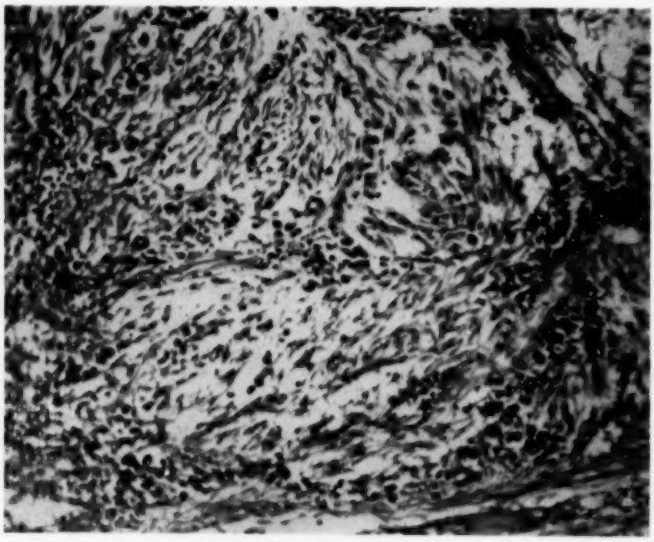

Fig. 2.—Deep portion of tumor, showing masses of ovoid and spindle cells. Black masses represent melanin deposits. Hematoxylin-eosin stain; mag. approx. × 500.

months or less. Two patients with melanomas occurring in polyps lived more than 20 months, and two others with lesions originating in hemorrhoids or anal tags were alive 8 years after diagnosis.[2]

Because of the relatively long period of survival in the present cases following only local excision, the slides were submitted to Drs. Arthur P. Stout and L. V. Ackerman, both of whom concurred in the original diagnosis. Dr. Stout further stated that he did "not know of any cases of malignant melanoma of the anal canal or anorectal junction that have been cured."

It would appear from the foregoing that the length of survival is more dependent upon the location of the tumor (submucosal, in polyps, in hemorrhoids, or in anal tags) or upon its biological characteristics than upon the type of surgical procedure employed.

Because of the foregoing considerations, Dr. Carl Moyer advised local excision rather than extensive surgery, and this advice was followed.

Summary

A case of malignant melanoma of the anorectal junction is reported in which the patient, a 65-year-old woman, is alive and apparently without recurrence or metastasis 43 months following only local excision of the lesion.

4500 Olive St. (8).

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Inadequate Operation for Pyloric Stenosis

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We have recently treated an infant who presented some of the diagnostic and therapeutic problems associated with inadequate initial surgery for congenital pyloric stenosis, and to emphasize this complication, which is rarely discussed, we are presenting the following case.

Report of Case

A 3-week-old male infant was admitted to the U. S. Army Hospital at Igloo, S. D., on May 7, 1956, because of persistent vomiting of three days' duration.

At birth he was a normal, full-term, 8 lb. (3629 gm.) infant, who had been delivered spontaneously from an occiput-anterior position under saddle-block anesthesia after an unremarkable multiparous labor. After a five-day normal hospital course he was sent home on an evaporated-milk formula, which he tolerated well until vomiting began, four days prior to the present admission. Formula changes at home by his mother had no effect on the vomiting, which became more frequent and profuse, and on the day of admission no feedings were retained. He had had no bowel movements for 72 hours. An enema at home had produced only small amounts of yellow-brown stool.

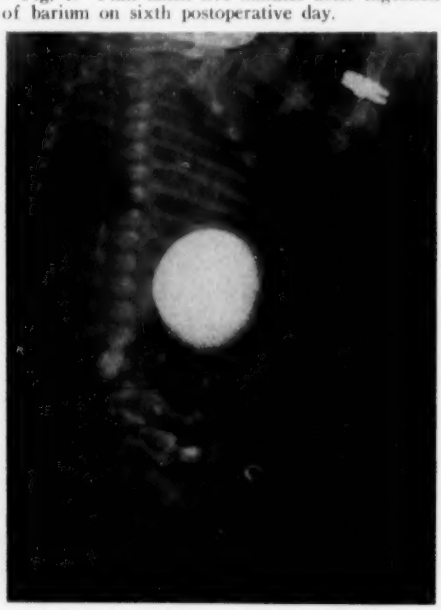
Family History.—One 3-year-old brother had been under the care of a pediatrician for persistent vomiting, which despite numerous formula changes was unrelenting until he reached 3 months of age, when it subsided spontaneously.

Admission Notes.—Physical examination at time of admission revealed a temperature of 99 F (rectal) and a weight of 7 lb. 3¼ oz. (3282 gm.). The baby was a well-developed, alert male infant, showing only moderate loss of skin turgor. Deep palpation of the right upper quadrant revealed a movable, firm mass approximately 1×2 cm. in size. A presumptive diagnosis of pyloric stenosis was made, and the patient was admitted to the hospital.

Hospital Course.—For 48 hours after admission the patient was treated with oral and parenteral fluids, but all oral feedings were vomited. No bile staining was observed in the vomitus. On May 10 the patient was operated upon. With local anesthesia, through a muscle-splitting right rectus incision 3.0 cm. in length, the peritoneal cavity was entered, and the pyloric portion of the stomach was delivered into the wound. The diagnosis of pyloric tumor was confirmed by the firm, rounded hypertrophy of the pylorus. The serosa and superficial gristly muscle fibers of the anterior superior avascular surface of the pyloric region were incised, and the deep muscle fibers were then spread with a small Kelly hemostat until the mucosa appeared in the depths of the incision. It was then felt that an adequate opening had been made and that all the fibers which could be safely divided had been split. No bleeding was observed. The stomach was returned to the peritoneal cavity and the wound was closed in layers. The patient was returned to the ward, in good condition.

Oral feedings were begun on the morning of the first postoperative day. The feeding regime suggested by Gross[1] was employed, and the first two feedings of 5% dextrose and water were retained. The child vomited the third feeding, but the feeding schedule was maintained. On the

Fig. 1.—Film taken five minutes after ingestion of barium on sixth postoperative day.



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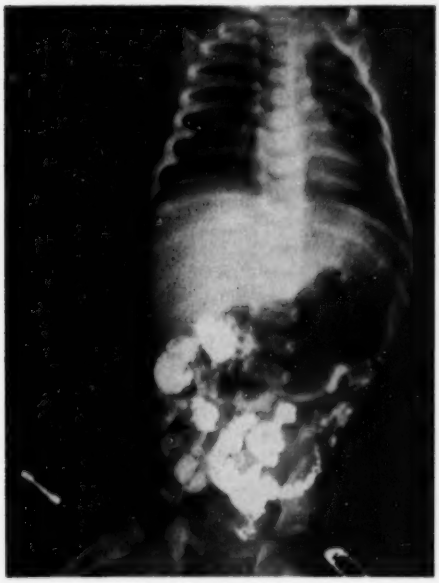
second postoperative day the patient was started on 2 oz. of a dilute evaporated milk formula every three hours. He vomited his first feedings, but repeated feedings of smaller amounts were retained. During the next three days the vomiting occurred frequently. We considered two possible explanations: (*a*) The surgery had not adequately relieved the obstruction, or (*b*) the child was exhibiting an intolerance to the formula. We gave the child barium sulfate by mouth on the sixth postoperative day. When the baby was placed on his right side for fluoroscopy, the barium was noted to enter the duodenum immediately. Figure 1 is a film taken five minutes after ingestion of barium and was interpreted as evidence that the pyloric opening was adequate. Further treatment was then based on the presumptive diagnosis of food allergy, and numerous changes of formula were made, with varying results. It was also noted that when certain nurses or the child's mother administered the formula the baby was less apt to vomit. We then felt that possibly poor feeding technique was contributing to the recurrent vomiting, and when an x-ray (Fig. 2), taken on May 28 (the 18th postoperative day), showed that all the ingested barium reached the colon the child was sent home on trial under his mother's care.

At home the baby at first gained weight, going from 6 lb. 8 oz. (2948 gm.) to 6 lb. 11 oz. (3033 gm.). For several days he retained most feedings or refeedings and continued to have normal bowel movements at least three times a day. The mother weighed the child each morning and called to inform us as to the frequency of vomiting, number of bowel movements, and the child's general appearance.

Fig. 2.—Film taken several hours after administration of barium on 18th postoperative day.



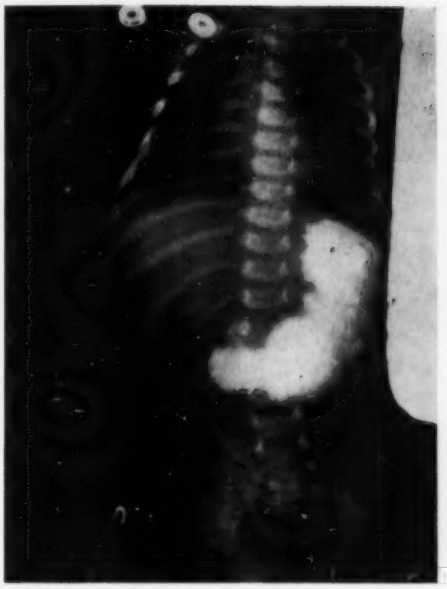


Fig. 3.—Film taken after ingestion of barium five weeks after initial operation.

We continued to temporize as long as the child gained or maintained his weight. However, on June 10 the baby began to vomit every feeding and his weight fell from 6 lb. 10 oz. (3005 gm.) to 6 lb. 8 oz. (2948 gm.). He was, accordingly, readmitted, and barium swallow on this occasion showed complete obstruction of the pylorus (Fig. 3).

He was treated with parenteral fluids and ascorbic acid, and on June 14, five weeks after the first operation, reoperation was performed.

The operation was again performed under local anesthesia. When the pylorus was delivered into the wound, there was no visual evidence of the previous incision. The serosal layer had healed completely. However, on palpation of the anterior superior aspect, a linear defect, estimated at about 1 mm. in width, could be palpated beneath the serosa. This confirmed our impression of a recurrent obstruction due to healing of the incision in the first operation. Accordingly, a new incision was made about 0.5 cm. inferior to the original incision on the anterior aspect of the pylorus. Care was taken to split all the muscle fibers from the duodenal to the gastric end of the stenotic region. The fibers were then spread widely with

a blunt hemostat so that the mucosa pouted well into the incision. No bleeding was observed, and the pylorus was then returned to the peritoneal cavity and the wound was closed in layers with the additional support of wire sutures carried through the anterior rectus sheath and rectus muscle.

Postoperative feedings were begun on the evening of operation. Again, Gross' regime was followed. The baby vomited his first dextrose and water feeding, but he vomited no other feedings. On the second postoperative day he was taking 2 oz. of formula every three hours, and on the fourth postoperative day he was taking pabulum and 3 oz. of formula every four hours with no regurgitation. No antibiotics were given, and he was afebrile through his entire hospital course. He was discharged on the sixth postoperative day, at which time his weight was 6 lb. 14 oz. (3118 gm.).

When he returned, on the 10th postoperative day, for the removal of the wire sutures, his mother reported that he had not vomited since his discharge. Weight on that day was 8 lb. (3624 gm.). The wound was well healed. Six weeks after the second operation weight was 11 lb. 11 oz. (5301 gm.). No vomiting had occurred, and physical examination was within normal limits.

Comment

We believe that this case demonstrates the typical confusion of symptoms and the surgical procrastination that arise after an inadequate Ramstedt procedure. A review of the literature [2-5] reveals very nearly complete absence of any discussion of this complication. While the inadequate operation is very rare in the pediatric centers reporting their results, it is our opinion that it has a much greater incidence. The great majority of these procedures are performed by surgeons with infrequent exposure to the problem. Their approach is undoubtedly influenced toward conservative surgical handling of the pyloric musculature because of the persistent warning by authorities on the matter that duodenal perforation is the major pitfall of the operation. We feel that the emphasis in the literature on avoiding perforation of the duodenum should be coupled with equally strong advice on performing an adequate operation. Unless the hypertrophied muscle fibers are thoroughly divided and separated so that the mucosa pouts well into the incision through the entire length of the stenotic region, the operator has not performed a complete operation. We suggest that the snare of an incomplete procedure is commoner than most operators appreciate and that the consequences can be equally serious and associated with a high mortality.[6] The diagnosis of perforation is usually apparent, while that of an inadequate operation is many times clouded by misinterpretation of the symptoms and x-ray findings, as well as the natural reluctance of the surgeon to admit that his operation was unsatisfactory.

Summary

A case of inadequate surgery for pyloric stenosis in a 3-week-old infant is described. The difficulties in management during the ensuing five-week postoperative course prior to a second adequate and successful operation are emphasized.

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Fatal Intracardiac Embolization from Indwelling Intravenous Polyethylene Catheter

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Embolization by an indwelling intravenous polyethylene catheter used for prolonged parenteral infusion has been reported previously.[1,2] The importance of this problem pointed up by a case of my own prompted this report. An abstract of the case follows.

Report of Case

A 33-year-old white man, a butcher, was admitted with a three-day history of abdominal pain, nausea, vomiting, and constipation. The history and physical examination were indicative of acute appendicitis with peritonitis. At operation a perforated gangrenous appendix with generalized peritonitis was found. The appendix was removed and the stump inverted into the cecum. The incision was closed in layers without drainage with interrupted silk sutures. The postoperative course was stormy and febrile, with daily temperatures to 103 or 104 F.

Ten days later the patient was reoperated upon because of intermittent small-bowel mechanical obstruction secondary to adhesions, unrelieved by intestinal intubation. These adhesions were lysed. A large collection of approximately 2 to 3 liters of pus and blood was found in the right lateral gutter posterior to the colon, and this was drained through a separate lateral stab wound.

From the time of admission the patient received large amounts of penicillin, streptomycin, and oxytetracycline U. S. P. (Terramycin) successively. After the second procedure, the oxytetracycline was discontinued, and he was treated with chlortetracycline (Aureomycin).

On the sixth postoperative day, following the second operation, some stay sutures were removed from the second wound because of obvious wound infection. Two days later a polyethylene catheter which had been placed in an antecubital vein in the right arm, and through which the patient had been receiving parenteral fluids and antibiotic therapy, disappeared. A house officer, after exploring the patient's bedclothes and clothing without finding the catheter, made two additional incisions more proximal to the cut-down in the antecubital fossa, in an attempt to locate the catheter in the more proximal portion of the vein, all without success. Repeated x-rays of the arm and chest were uninformative.

The following day it was noted that the initial laparotomy incision showed incomplete dehiscence, with a loop of small bowel protruding at its upper angle. This was packed with sterile petrolatum (Vaseline) gauze and strapped closed. Two days later fecal drainage was noted from the right iliac stab wound, through which the Penrose drains emerged. A small-bowel loop was also noted protruding in the upper end of the patient's second incision. This, too, was packed with sterile petrolatum gauze and sponges and strapped tight. At this time the patient was jaundiced and extremely anorexic and asthenic, with his temperature still spiking to 102-103 F daily. His abdomen later the same day became distended, requiring an indwelling Cantor tube and constant suction. A second polyethylene catheter was placed in the opposite arm for parenteral infusions and antibiotic therapy.

On the following day thrombophlebitis necessitated removal of this catheter. The next day, which was the patient's 24th hospital day, he was noted to be passing tarry fecal material through the stab wound, and several tarry bowel movements were noted per rectum.

The patient continued to have a spiking fever and passed tarry stools for several days thereafter. Repeated x-rays of the chest at this time showed elevation of the right diaphragm, and a presumptive diagnosis of a subphrenic abscess was made (Fig. 1). The patient appeared to be deteriorating rapidly. The right upper quadrant and perihepatic areas were explored for abscesses, with negative results. His temperature continued to spike to 104 F after this last procedure. He also began to complain of dyspnea and developed a cough productive of clear white sputum. Bronchoscopy was negative. The patient's antibiotic therapy at this time was changed to bacitracin. However, the urinary sediment revealed many granular casts and white cell casts within the next few days; so

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Fig. 1.—X-ray of chest showing elevation of right hemidiaphragm.

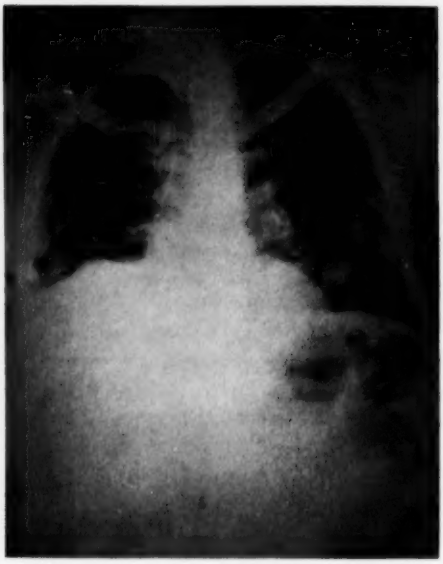


Fig. 2.—X-ray of chest showing scattered hazy infiltrates in left lung.

bacitracin was discontinued and a broad-spectrum antibiotic was reinstituted.

On the 35th hospital day x-rays of his chest revealed spotty infiltration of the left lung. This was 17 days after the unexplained disappearance of the inlying intravenous polyethylene catheter (Fig. 2).

On the following day rectal examination revealed a pelvic mass, which was firm, had no areas of fluctuation, and was markedly tender. Blood cultures at this time were reported to contain Staphylococcus aureus, coagulase-positive. After this, he developed a very loose cough productive of blood-streaked sputum, which soon became purulent. X-rays of his chest revealed moderate elevation of the right diaphragm and pleural thickening at the right base. The impression was that the lesions were metastatic pulmonary abscesses. In view of these findings and the septic course, it was thought that he most likely had a pelvic suppurative endophlebitis with septic embolization to the lungs. Consequently, extraperitoneal ligation of the inferior vena cava was done. Postoperatively, he did well except for the fact that he continued to have a spiking fever, as before. The lower extremities did not enlarge.

Sensitivity tests on repeated positive blood cultures showing S. aureus, coagulase-positive, revealed the organism to be sensitive to chloramphenicol (Chloromycetin) and bacitracin. Consequently, the patient was started on chloramphenicol, 500 mg. every four hours, again without evidence of clinical improvement.

The patient continued to have a spiking fever and to waste away, without particular improve-

Fig. 3.—X-ray of chest showing increasing consolidation of right lung and confluence of left lung lesions.

ment in symptoms of productive cough and dyspnea.

X-rays of the chest on the 61st day, 18 days following the vena cava ligation, revealed a marked increase in extent of the consolidated areas formerly seen in the left lung, and it was also noted that the central lung field on the right was incompletely consolidated (Fig. 3). There was a pleural effusion on the right, extending to the level of the seventh rib in the midaxillary line, as well as elevation of both domes of the diaphragm.

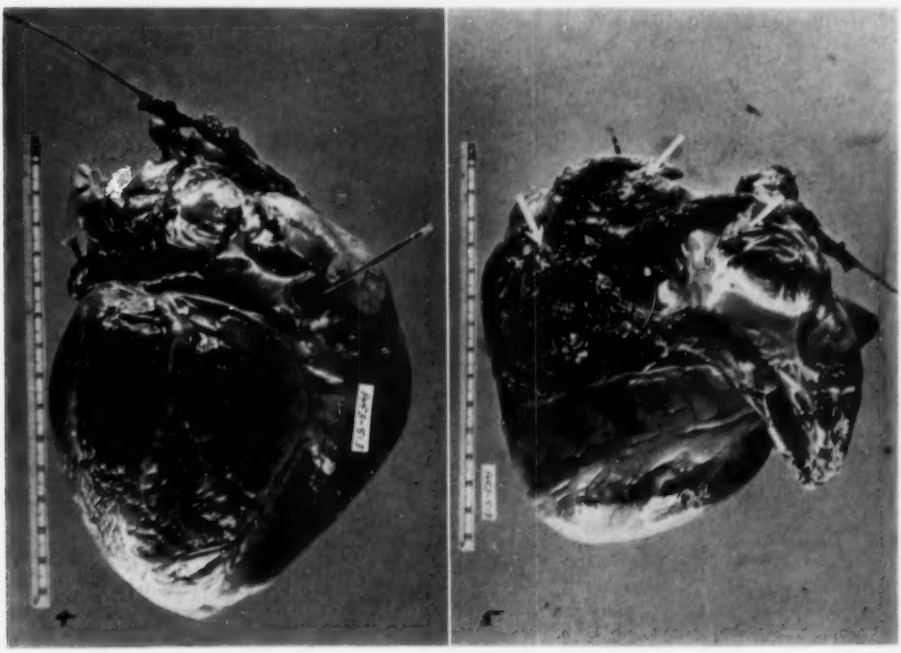
On the following day, the patient seemed more dyspneic than usual and was hyperventilating. Blood chemistry determinations done on that day revealed BUN 77 mg. per 100 cc., CO_2 11.4 mEq/L., chlorides 77 mEq/L., and hematocrit 15%. The patient was dehydrated and was thought to have a low-sodium syndrome. He was treated vigorously with rapid digitalization, placed in an oxygen tent, and given molar lactate solution and whole blood. Bacitracin-chloramphenicol combinations were also given. The EKG was unremarkable. The following day the patient appeared improved slightly. The CO_2 was 16.4 mEq/L., BUN 72 mg. per 100 cc., serum sodium 136.5 mEq/L., chlorides 102 mEq/L., and potassium 6.4 mg. per 100 cc. Urinary chlorides were 26.7 mEq/L., with a total urinary output for the day of 200 cc. The following day, his urinary output was low, and his lungs contained rhonchi and multiple moist rales bilaterally. The next morning he quietly died.

At autopsy the findings of multiple pulmonary abscesses were established. Lying in the right heart was the polyethylene catheter, with extensive acute bacterial endocarditis in and around it, the obvious source of the multiple pulmonary abscesses (Figs. 4 and 5). The abdominal wounds were relatively well healed, and, except for multiple intra-abdominal adhesions, there was nothing else of note. The vena cava had been ligated and exhibited no extension of a thrombus, either proximal or distal to the point of ligature.

Comment

This case represents a tragedy resulting from a large blind spot in our experience, and, although an uncommon occurrence, one of extremely serious import for a procedure which is used so commonly, and, I believe, without due regard for the dangers inherent in its use. An otherwise very complicated case of ruptured appendix probably would have been salvaged.

Figs. 4 and 5.—Photographs of heart showing catheter in situ in right auricle and ventricle. Arrows point to areas of acute endocarditis.



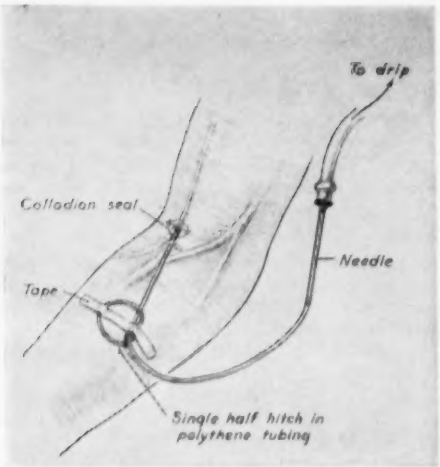


Fig. 6.—Line drawing demonstrating method of inserting and tying polyethylene catheter.

My colleagues and I now insist on the following routine precautions whenever an indwelling polyethylene catheter is to be used.

1. A completely sterile technique is used (gowns, gloves, and mask). This will prevent in large part the phlebitis so commonly seen following this procedure, and thus allow the intravenous catheter to remain in place much longer.

2. In addition to a suture tied around the catheter as it enters the skin, a single "loop" knot, or "half-hitch," is taken in the catheter itself before attaching it to the needle and adapter leading to the infusion bottle (Fig. 6). This thereupon knots itself into a large loop knot if pulled, and consequently prevents the catheter from being drawn into the vein. In addition to this, inasmuch as it is theoretically possible to have the above "knot" untie itself, a drop of collodion is placed on the catheter as it enters the skin, thus adding an additional block to the catheter's being slipped up into the vein.

3. The usual taping of the excess catheter to the skin is done but, as shown in the case presented here, is not to be relied on.

4. Small amounts of a dilute solution of heparin to keep the catheter patent are likewise used routinely.

In addition to the above routine now used on our service, we believe that if the catheter could be made radiopaque, an instant answer to the problem would be made available by x-ray. Certainly, it is obvious that a simple transappendicular atriotomy would have been curative and life-saving if we had had x-ray evidence of where the catheter was residing or had been sufficiently astute to appreciate the true pathogenesis of the multiple pulmonary abscesses.

Summary

A case ending fatally as a result of embolization into the heart of an indwelling intravenous polyethylene catheter is presented. Precautions to be used in avoiding this tragedy in a procedure widely and commonly practiced are recommended.

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Soft-Tissue Sarcoma of the Shoulder. with Thirty-Six Years' Survival

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Harrington,[1] from the Mayo Clinic, gives a statistical report of 4563 cases of 15 to 40 years' survival following radical mastectomy for cancer of the breast. Thirty-five of these patients lived 35 to 40 years following radical mastectomy.

Morton and Morton[2] report from the University of Rochester (New York) 17 cases of cancer originating in various organs in which incomplete surgery was done. The average length of survival was 12.2 years. Two of the patients survived 24 and 26 years, respectively.

Stout[3] cites a case reported by Harper and Feder[4] of survival 50 years after onset of symptoms of a rhabdomyosarcoma of the neck.

Gordon-Taylor[5] reports a case of spindle-cell sarcoma of the infraspinatus muscle in which the patient survived 32 years.

Grey's[6] patient survived 20 years after excision of a sarcoma of the vastus lateralis.

From the Brooklyn Cancer Institute we reported a case of lymphosarcoma of the intestine in a boy of 7 years who survived 22 years without recurrence or metastasis.[7]

Stewart[8] reports a case of spontaneous regression of an inoperable myosarcoma of the uterus that spread throughout the pelvis and mesenteries. The tumor was not radiosensitive. The patient developed a high fever and urticarial rash and a high eosinophilia, and within a few days lost kilograms of tumor and ascitic fluid. The tumor disappeared completely. The author also cites the case of a woman with metastatic carcinoma from an ovary that had been removed 35 years previously.

Stewart also records a case of reticulum-cell sarcoma of the femur for which amputation at the lower end was performed. The disease recurred throughout the entire length of the remaining femur, associated with metastases to the skin of the abdominal wall. All disease vanished under treatment with Coley's toxins (unfiltered mixture of erysipelas and Bacillus prodigiosus (Serratia marcescens) toxins) alone, and the patient was well 30 years later. The all-time record for behavior of cancer, according to Stewart, is the case of a cylindroma in which the tumor was first noticed at the age of 15 and first operated on at the age of 29, and the patient died at the age of 80.

A new case of sarcoma of the shoulder in which the patient is living and well 36 years after onset of symptoms is here reported.

Report of Case

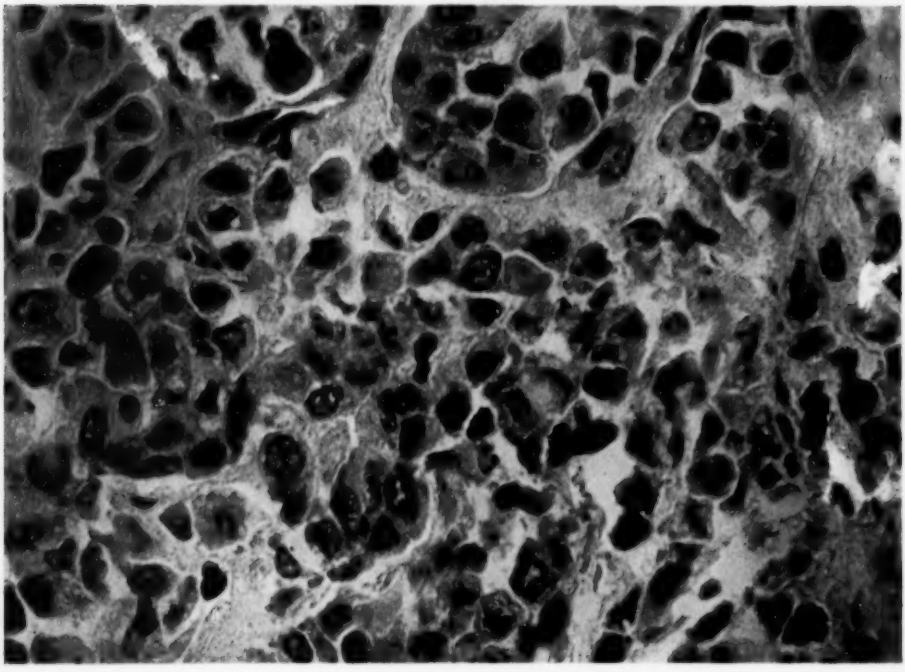
A white woman, aged 35, was admitted to the Brooklyn Cancer Institute (now the John E. Jennings Hospital) in December, 1930, complaining of pain, marked swelling, and inability to raise her right arm, and of ulceration and bleeding from her right shoulder (Fig. 1).

Pain first developed in her right shoulder in 1920; her family doctor made the diagnosis of "rheumatism" and gave her some medicine. She continued the medication for a year, at which time she noticed a hard lump at the right shoulder the size of a "drinking cup." She was admitted to a hospital in 1921, where the tumor was removed, followed by x-ray therapy. Six months later a nodule the size of a plum appeared at the operative scar. This was excised in 1923, and she was again given x-ray therapy.

Six years later the growth reappeared for the third time, accompanied by another growth in the right axilla. This time she had radium implanted in the tumor, followed by a third course of x-ray therapy. The growth appeared to subside somewhat, but shortly afterward it began to grow very rapidly, until it reached the size of a large grapefruit. She was admitted to a hospital, where

Fig. 1.—Patient with ulceration and necrosis of large round-cell sarcoma and lymphedema of the right arm.

Fig. 2.—Photomicrograph showing large round-cell sarcoma.



the tumor was removed, with resulting ankylosis of her right shoulder joint, continual drainage of pus and blood from the wound, and subsequent recurrence of the tumor for the fourth time.

On April 8, 1930, she was taken to Bellevue Hospital, where the tumor was removed for the fourth time, followed again by implantation of radium in the wound and a fourth course of deep x-ray therapy. The pathological report of the tumor, by Dr. Douglas Symmers, was that of a "richly cellular and vascularized sarcoma of a large round-cell type" (Fig. 2). X-ray examination of the right shoulder at this time revealed "absence of a portion of the head of the humerus with erosion of the glenoid fossa and obliteration of the joint space." On Oct. 27, 1930, she was treated in a hospital for erysipelas. Subsequently, on Dec. 1, 1930, she was admitted to the Brooklyn Cancer Institute.

Examination on admission revealed a 35-year-old white woman in extreme pain. The body was bent forward, being weighed down by the right upper extremity, which was more than twice the normal size and was supported by the patient's left hand. The right shoulder was the site of large, ulcerated, excavated areas, exposing part of the scapula and shoulder joint. The surrounding tissue was covered by a slough, discharging pus and blood. The right axilla had two large keloid scars, which held the right arm close to the chest. The rest of the physical examination was essentially negative.

Laboratory examination revealed the urine to be within normal limits. The red blood cell count was 4,200,000 with 63% hemoglobin. The white cell count was 6900, with 78% polymorphonuclears, 17% lymphocytes, 3% transitional cells, and 2% eosinophils. The blood Wassermann test was negative. The blood chemistry was within normal limits, and x-ray of the chest was negative for metastasis.

On Dec. 5, the patient was taken to the operating room, and the right upper extremity was removed by interscapular thoracic amputation without disarticulation, the arm being removed together with the scapula and the outer two-thirds of the clavicle. Complete closure of the wound was impossible because of the large defect left following the extensive tissue removal. The pathological report of the tumor was again "large round-cell sarcoma." She was discharged from the hospital on Jan. 8, 1931, with no evidence of any metastatic foci, and was readmitted a week later for a pinch graft. Two weeks later she was referred to the outpatient department for a fifth course of deep x-ray therapy.

In 1932 an ulceration developed at the site of the operative scar, exposing part of the fourth rib and discharging purulent material. X-ray revealed the presence of a sequestrum in the fourth rib. On July 21, 3 in. (7.5 cm.) of the fourth rib was removed. The pathological report was "necrotic osteomyelitis." Between Oct. 5, 1932, and March 1, 1933, she received sixth and seventh courses of radiotherapy, followed shortly by another ulceration. The ulceration healed within a year.

By 1937 a bronchocutaneous fistula developed. Operation was recommended, but the patient refused and failed to return.

The patient was seen again on Oct. 30, 1956. She stated that she had treated herself at home until one day she noticed "maggots" crawling in the wound. She was admitted to another hospital on Oct. 29, 1953, where preoperative x-ray of the chest showed fibrosis of the right upper lobe with osteomyelitis of the sixth and seventh ribs on the right side. According to the transcript of her record, "after five days of chemotherapy the right upper ribs were resected, and the chest wall defect, together with the bronchocutaneous fistula, was closed by mobilizing the skin flaps and intercostal muscle bundles, and also utilizing the right breast. She was discharged from the hospital on Dec. 28, 1953" (Fig. 3).

Fig. 3.—Patient 36 years after onset of symptoms.

The patient was last seen on Dec. 7, 1956. The only complaint she had at that time was intermittent dyspnea on exertion. Examination revealed no evidence of recurrence or metastasis. The photomicrographs were submitted to Dr. Arthur Purdy Stout, who confirmed the malignancy of the tumor.

Summary

A case is presented of a 35-year-old woman who had a large round-cell sarcoma of the shoulder and has survived 36 years after onset of symptoms. She had had four local excisions and four recurrences. She also received four courses of deep x-ray therapy and two implantations of radium within a period of 10 years, at which time she had no metastasis, in spite of the tumor being highly malignant. At the end of that period she developed erysipelas severe enough to be hospitalized. After 10 years the patient's shoulder and arm became ulcerated and necrotic and began to slough. The lymphedema of the arm became so severe that it weighed the patient down. An interscapular thoracic amputation without disarticulation was performed. She subsequently received three more courses of deep x-ray therapy. The patient is now living and well, 36 years after onset of symptoms.

In another communication [9] it was asked editorially, "Why do some cancer patients die when they are expected to live and others live for many years when they are doomed to die?" The answer given was that we are all "born with an anticarcinogenic factor which holds the aberrant tissue [of Connheim] under control; combats, prevents, retards and destroys tumor formation. When a malignant tumor does form and is subsequently removed, . . . metastasis is retarded or prevented by the anticarcinogenic factor." Hence one patient will survive for many years without metastasis while another with the same kind of disease, treated in the same manner, will die with generalized metastasis in a surprisingly short time. Our patient has an abundance of anticarcinogenic factor; hence she is alive, 36 years after the onset of symptoms. Crile [10] and others call this factor cancer resistance. Stewart calls it growth control and states: "If we knew wherein this control exists, we would have gone a long way toward the answer of cancer."

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Echinococcus Cyst

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Introduction

Hydatid disease is rare in the United States, and an Echinococcus cyst occurring in the thigh muscles is rarer yet. At the Veterans' Administration Hospital, Cleveland, a case was encountered in 1952 in which a large cyst was found in the posterior thigh muscles and was surgically excised. This was the only case found clinically in some 76,308 admissions in the 10 years that the hospital has been open. During this same period 2611 autopsies* have been performed, and among them 3 other Echinococcus cysts, all of the liver, were encountered as incidental findings in patients who died of other conditions. On account of the rarity of reported cases of Echinococcus disease in this country, and because of the scarcity of references to it in the recent English literature, it appears worth while to report our case in detail.

Report of Case

A 60-year-old white man, a laborer, was admitted to the hospital Feb. 9, 1952, complaining of a large mass in the right leg, of three weeks' duration. This was first noted by his wife in the posterior aspect of the right thigh and was painless until about 10 days before admission, when he noted mild, nonradiating pain in the region of the mass. He stated that he had noted a similar mass in the same area about five years before admission but that it had disappeared on bed rest. He had noted no masses elsewhere. There was no recent weight loss. Two years before the present admission he had had a gastric resection for peptic ulcer in this hospital; physical examination at that time showed no evidence of any lesion of the right thigh. The patient had worked all his adult life in the steel mills and the building trades. While in the U. S. Army in the First World War he was in Siberia and the Philippines. He had no association with dogs or sheep in Siberia but did have contact with dogs while in the Philippines. He was born May 3, 1892, in the town of Sibenik on the Dalmatian coast of Yugoslavia. Sibenik is presently a city of about 16,000 inhabitants. As a boy the patient lived in the town but worked on a farm part of the time. This farm had 300 to 400 sheep and dogs, which frequently were fed offal from slaughtered sheep. At the age of 17 he moved to the United States and had lived in northeast Ohio to the present time. There was a long past history of repeated hospitalizations, both elsewhere and in this hospital, for the repair of inguinal hernias and the treatment of duodenal ulcer.

On physical examination the temperature, pulse, and respiration were found to be normal. The blood pressure was 140/80. He appeared to have lost some weight and was apprehensive. Except for several old abdominal scars and a right inguinal hernia, the general physical examination was not remarkable. There was a 10×8 cm. mass in the right posterior thigh in the midline occupying the midportion of the thigh. It appeared to be, at least in part, posterior to the muscles. It was not tender and was of limited mobility. It was firm but not stony-hard. No bruit or murmurs could be made out.

The hemoglobin was 12.45 gm. per 100 cc. The white blood cell count was 7900, with 70% neutrophils, 21% lymphocytes, 5% monocytes, 3% eosinophils, and 1% basophils. A repeat white blood cell count about two weeks after operation was essentially the same. Urinalysis and serology were negative. Sputum examination for acid-fast organisms was negative. The serum thymol turbidity, alkaline phosphatase, acid phosphatase, CO_2, sodium, potassium, chlorides, total protein, and albumin-globulin ratio, and BUN all were within normal limits. The sedimentation rate was 34 mm/hr. The roentgenogram of the chest showed a granular appearance of the lung fields consistent with pneumonoconiosis. The roentgenogram of the right thigh revealed a large mass without evidence of calcification in the soft tissues of the thigh posteriorly in the region of the middle third of the

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* About half of these were made on patients who died in this hospital, the rest on patients dying in four other Veterans' Administration Hospitals in this area.

Fig. 1.—At operation the cyst has been partially dissected free from surrounding tissue in the thigh.

femur. Gastrointestinal roentgenograms were reported as showing a subtotal gastrectomy with a functioning gastroenterostomy. There was no evidence of marginal ulceration. The skeletal survey was essentially negative except for arthritic changes in the lumbar spine and in the sacroiliac and hip joints. The skin test and complement-fixation test for Echinococcus disease were not carried out.

On Feb. 20, 1952, the patient was taken to the operating room and, with gas-oxygen-ether anesthesia, the thigh was explored. There was a large multilocular cyst located between the bellies of the semimembranosus and semitendinosus and biceps femoris muscles. The sciatic nerve was stretched over the posterior aspect of the cyst. The cyst apparently arose from and was partially incorporated in the body of the adductor magnus muscle and extended from the ischial tuberosity to the posterior aspect of the knee. It was grayish white, had moderately thick walls, and was loosely attached to surrounding structures except in the region of the linea aspera, where separation from the bone was fairly difficult. During the dissection a small opening was inadvertently made in the cyst, with the escape of thick, yellow, odorless material containing numerous small structures having the appearance of grape pulps. This opening was immediately closed with a suture, and after removal of the cyst the wound was meticulously irrigated with saline. The wound was closed with silk, and the patient made an uneventful recovery. When seen at follow-up in February, 1956, he had remained asymptomatic and showed no evidence of recurrence.

Gross pathological description of the mass was as follows:

"The specimen consists of a multilocular, irregular cyst that measures 21×10×3 cm. The largest cyst cavity has a circumference of 10.5 cm. and a pale, gray, firm, fibrous wall, which

Fig. 2.—Low-power view of the cyst wall (crossing the lower portion of the photograph). In about the midportion and near the inner surface can be seen a hooklet. Above this, occupying the upper portion of the photograph, is a cross section of a daughter cyst. Reduced to 61% of mag. × 12.

Fig. 3.—Higher-power view of hooklet seen in Figure 2. Beneath it is shown the cyst wall, made up of hyalinized fibrous connective tissue. This tissue, also known as the adventitia, is elaborated by the host to surround the cyst. Reduced to 61% of mag. × 100.

Fig. 4.—Higher-power of a portion of daughter cyst to show laminated chitinous material. Reduced to 61% of mag. × 100.

measures 0.3 cm. in average thickness. Numerous tube-like, irregular cysts project from the main cyst. The external surfaces of the cysts are dull reddish-gray and covered with numerous irregular, small, fibrous tags. Section of the specimen reveals abundant soft, pale, gray material and numerous free-floating smaller cysts, which measure up to 1.4 cm. in diameter. Section of these small cysts reveals that they contain clear fluid and have a thin, translucent to semiopaque, pale gray, fibrous wall. The inner surfaces of the larger cysts are irregular, finely granular, and pale gray."

Comment

The Echinococcus granulosus is a parasite of dogs, wolves, jackals, foxes, cats, and other carnivorous animals. Cattle and sheep are the usual intermediate hosts, but man may also become infected. The disease occurs in parts of Central Europe, and in North and South Africa, South America, Arabia, Siberia, Turkestan, North China, Japan, and the Philippines.[14] In 1940 world incidence was highest in Australia, New Zealand, Uruguay, and Argentina.[14] There are no important endemic foci in the United States.[14] Of 519 cases found by Magath [11] in 1941, reported from North America (except for Mexico and Alaska), 95% of the patients contracted their disease in foreign countries. Magath [10] further states that less than five cases a year are observed in the United States and Canada and only about one native case in five years in these countries.

The adult worms, which live in the small intestine of the dog, measure 3 to 8 mm. in length and are made up of a scolex having suckers and hooklets and three to four successively larger segments. The ova are excreted in the feces and gain access to cattle and sheep through contaminated fodder or water.[11] Ova gain access to man, and infestation oftenest occurs in childhood [5] from water and close relationship with infected dogs. Man is parasitized by the larval, or hydatid, stage only. The eggs hatch in the gastrointestinal tract, and within a short time the larvae enter the blood stream, passing usually to the liver. They may, however, be carried to other organs; in a series of 2700 cysts cited from Deve by Dew,[5] the sites of cysts are listed in the accompanying Table.

*Location of Cysts in 2700 Cases**

	Per Cent		Per Cent
Liver	76.6	Spleen	2.1
Lung	9.4	Bones	0.9
Muscular and cellular tissue	5.2	Orbit	0.7
Kidney	2.3	Brain	0.6
		Miscellaneous	2.2

* Cited from Deve by Dew.[5]

The cysts, if unruptured, may produce injury as a result of pressure. Liver cysts may be asymptomatic until some complication compels the patient to seek medical advice. Several such complications have been listed by Dew.[5] These are (1) rupture into the bile ducts with cholangitis and jaundice, (2) suppuration of the cyst content, (3) intraperitoneal rupture, (4) intrathoracic rupture, (5) rupture into the alimentary canal, and (6) rare forms of rupture and extension. If the cyst ruptures either spontaneously or as a result of manipulation, there may be a violent anaphylactic reaction, which in some cases is fatal. Pulmonary involvement may cause cough, slight hemoptysis, and transient fever. These cysts are also subject to the complications of rupture and infection, as are the liver cysts.

The diagnosis is made with certainty by examination of fluid from the cyst and the finding of scolices or hooklets. Excision of a cyst or a portion of a cyst and the finding of curled, laminated cyst wall on microscopic section are also diagnostic.[14] The finding of calcification in a cyst wall in the pulmonary region, and especially in the liver area, by roentgenography is suggestive. The cutaneous allergic test (described by Casoni in 1911) and the complement-fixation test are said in Australia to give 85% positive results.[13] The Casoni test will remain positive many years after the cyst is removed, possibly for life, while the complement-fixation test remains positive only as long as the living cyst is present in the host.[11] Eosinophilia is present in only 20%-25% of cases.[14]

Treatment is surgical, there being no known drug which will penetrate the cyst and destroy the parasites.[6] Wherever possible, complete surgical excision should be carried out without spillage of cyst contents; this can usually be done in the case of lung, muscle, and soft-tissue cysts. Small, uncomplicated liver cysts, too, usually can be completely excised, and, according to Fitzpatrick,[9] the residual cavity in the liver should be closed. Larger and complicated liver cysts first are aspirated and then removed, and the space filled with saline and closed without drainage.[9] If these cysts are infected (usually with a Staphylococcus of low virulence), the inside is scrubbed with a formalin swab, irrigated with saline, and closed.[9] Fitzpatrick states he tries never to drain an adventitial cavity to the outside if he can help it. He feels, also, that it is unwise and unsafe to inject formalin directly into a cyst. If a cyst has ruptured into the biliary tree, producing common-duct obstruction (frequently due to daughter cysts), this must be treated, as well as the liver hydatid.

Summary

1. Hydatid disease is rare in the United States.

2. A case of a large hydatid cyst in the thigh treated by surgical excision is presented and the disease discussed.

Dr. W. A. Morningstar, Assistant Chief, Laboratory Service, Veterans' Administration Hospital, Cleveland, provided the pathological description of the gross specimen and selected and interpreted the photomicrographs.

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Recurrent Gastrojejunal Ulceration and Islet-Cell Carcinoma of the Pancreas

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The surgical treatment of the complications of duodenal ulcer produces good results in the majority of patients, for only 2% to 5% of such operations fail to relieve the ulcer symptoms. Furthermore, many of the patients who subsequently develop marginal ulceration may obtain permanent relief by further medical management or additional surgical procedures. However, there remains a small group of patients who have such a propensity to develop peptic ulceration that subtotal gastrectomy with or without vagotomy fails to alter the course of the disease, and in some total gastrectomy has been necessary. The etiologic factors which separate these patients from the usual ulcer patient have not been clearly delineated in the past. Consequently, the reports by Ellison and Zollinger concerning the association of non-insulin-producing islet-cell tumors of the pancreas and recurrent peptic ulceration have stimulated interest in the possible relationship of these two lesions.[1,2] We have recently encountered a patient with an islet-cell carcinoma of the pancreas who exhibited recurrent gastrojejunal ulceration.

Report of Case

A 34-year-old Negro man was first admitted to the Veterans' Administration Hospital, Houston, Texas, on March 3, 1950, complaining of intermittent, burning, nonradiating epigastric pain of nine months' duration. Alkali, milk, and food offered temporary relief. On occasion there was associated nausea and vomiting, as well as abdominal distention, which was relieved by eructation. There had been no weight loss.

Physical examination revealed a well-developed, well-nourished Negro man weighing 156 lb. (70.8 kg.). There was moderate epigastric tenderness without rebound tenderness or muscle guarding; no organs or masses were palpable. The hemoglobin, hematocrit, urinalysis findings, and roentgenogram of the chest were within normal limits. A fasting specimen of gastric juice contained 95 mEq/L. of total and 80 mEq/L. of free hydrochloric acid. A roentgenogram of the upper gastrointestinal tract following the ingestion of a barium meal disclosed an irritable and deformed duodenal bulb, without evidence of an active ulcer. The patient became asymptomatic on a medical regimen and was discharged on April 6.

He limited his diet to milk, cereal, eggs, and toast, but symptoms rapidly recurred, so that he was readmitted on Aug. 9, 1950, having lost 14 lb. (6.4 kg.) in weight. Examination revealed slight epigastric tenderness with questionable rigidity. On this occasion a fasting specimen of gastric juice contained 113 mEq/L. of total and 105 mEq/L. of free acid, and a roentgenographic study of the upper gastrointestinal tract following ingestion of barium disclosed an ulcer niche in the duodenum with slight gastric retention. Medical therapy was again instituted, with complete relief of symptoms, and the patient was discharged on Oct. 18, 1950.

He remained asymptomatic for a few months, but symptoms again recurred; and on Oct. 18, 1951, he was admitted to another hospital, where a diagnosis of duodenal ulcer with pyloric obstruction was made. On Dec. 7, 1951, a partial gastrectomy was performed, reconstituting gastrointestinal continuity with a gastrojejunal anastomosis. The patient was discharged on Jan. 4, 1952.

He was readmitted to the same hospital on Aug. 27, 1952, because of recurrent, persistent, burning epigastric pain, with tenderness to deep palpation in the epigastrium. Laboratory studies were again within normal limits except for a fasting gastric analysis, which revealed 68 mEq/L. of total and 48 mEq/L. of free acid. Determination of gastric acidity following insulin administration

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was reported to show a maximum of 118 mEq/L. of free acid. A fasting blood sugar performed on this admission was 68 mg. per 100 ml. A roentgenogram of the stomach following ingestion of barium revealed no evidence of marginal ulcer, and gastroscopic examination showed a granular and hyperemic gastric mucosa. However, it was felt that the diagnosis of marginal ulcer was not excluded by these two determinations, and on Sept. 10, 1952, a transthoracic vagotomy was performed. The gastric drainage was recorded as 1500 ml. during the first 24 hours after surgery, and a fasting sample of gastric juice contained 32 mEq/L. of total and 4 mEq/L. of free acid, with a maximum response of 75 mEq/L. of total and 59 mEq/L. of free acid following insulin injection. The patient was discharged from this hospital on Sept. 23, 1952.

Following this admission the patient remained essentially asymptomatic for three and one-half years, when his symptoms again recurred; and on June 8, 1956, he was admitted to the Veterans' Administration Hospital, Houston, Texas, complaining of a sudden onset of excruciating epigastric pain, five hours prior to admission. Examination revealed an acutely ill Negro man, weighing 147 lb. (66.7 kg.). The abdomen was acutely tender to examination, and there was board-like rigidity. A roentgenogram of the abdomen demonstrated free air in the peritoneal cavity.

A clinical diagnosis of perforated marginal ulcer was made, and this diagnosis was confirmed at the time of laparotomy, performed a few hours after admission. A small segment of stomach was removed with the attached portion of jejunum, and gastrointestinal continuity was reestablished by a jejunojejunostomy and end-to-side gastrojejunostomy. At the time of this exploration the surgeon reported that the pancreas was examined and no tumor was palpated. During the postoperative period 24-hour gastric drainage averaged 1200 ml.; however, his convalescence was uneventful, and he was discharged on July 5, with instructions to continue his treatment with a convalescent ulcer diet, antacids, and antispasmodics.

Severe epigastric pain with protracted nausea and vomiting recurred 11 days after discharge, and when this had persisted for four days he returned, on July 20. Examination revealed moderate tenderness in the epigastrium without rebound tenderness or rigidity. No organs or masses were palpable, and there had been no weight loss. The usual laboratory tests were again within normal limits. However, 24-hour gastric drainage averaged 1050 ml., and analysis of a fasting sample of gastric juice revealed 26 mEq/L. of total and 20 mEq/L. of free acid. The gastric drainage contained blood. When a roentgenogram of the gastric remnant following ingestion of barium disclosed a recurrent marginal ulcer, an intensive medical regimen was instituted and continued for one month. The patient failed to obtain relief of his symptoms; therefore, further surgery was deemed advisable, for, despite the fact that two gastric resections had been performed, a relatively large pouch could be visualized upon roentgen examination and the presence of free acid on analysis of a fasting sample of gastric juice suggested an incomplete vagotomy. The possibility of an associated pancreatic tumor was discussed but was felt to be excluded by the fact that the pancreas had been explored at the time of surgery in June, 1956.

On Aug. 20, 1956, a laparotomy was performed. Upon entering the peritoneal cavity, large nodes were palpated at the root of the mesentery in the region of the celiac axis and in the pancreaticosplenic and gastrocolic ligaments. While the surgeon was proceeding to attack the stomach, one of these nodes was sent to the laboratory for microscopic examination. A subdiaphragmatic vagotomy was performed, and a further resection of the stomach was accomplished, leaving an estimated 10% of the stomach intact. The portion of the jejunum including the marginal ulcer was excised and gastrointestinal continuity reestablished as previously by an end-to-end enteroenterostomy and an end-to-side gastrojejunostomy. A frozen-section histological report on the biopsy specimen of the lymph node was "malignant neoplasm resembling argentaffin-cell tumor." Therefore, attention was directed to the pancreas, and there a tumor was found in the body. A thorough examination of the remainder of the pancreas revealed no other suspicious areas; therefore, an en bloc resection of the spleen and the tail and body of the pancreas, with division of the gland at the level of the superior mesenteric artery, was accomplished. In so doing, the large nodes in the gastrosplenic and gastrocolic ligaments were removed. Additional nodes were removed from the base of the mesentery and from the region of the celiac axis, so that all visible and palpable areas of tumor were removed.

The pathological examination was reported as follows: "The specimens removed included the pancreas, spleen, portion of the stomach and jejunum, segments of the vagus nerves, and lymph nodes. In the portion of stomach and jejunum at the gastrojejunostomy site was an erosion 1.5×1 cm., with a shallow base covered with necrotic debris. Microscopic examination revealed that one surface was lined by tall columnar cells, which dipped to form glands. This was contiguous with a fibrinopurulent exudate covering a zone of fibrinoid material on vascular granulation tissue, infiltrated with lymphocytes, plasma cells, large mononuclear cells, and neutrophilic granular sites.

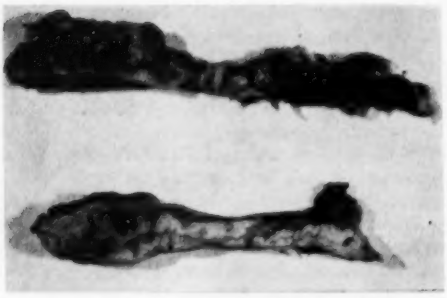


Fig. 1.—Gross appearance of the surgical specimen, showing a tumor in the pancreas and a lymph-node metastasis.

On the other side, tall columnar cells lined evenly spaced crypts.

"In the body of the pancreas there was a firm nodule 3.5×2 cm. in diameter. On cut surfaces gray-white neoplastic tissue was interspersed with calcific areas (Fig. 1). Microscopic examination revealed that the pancreatic tissue was replaced by uniform, closely spaced neoplastic cells and abundant, partly hyalinized connective tissue stroma. The neoplastic cells had oval, vesicular or small, deeply stained nuclei with a moderate amount of cytoplasm. Some neoplastic cells palisaded around blood vessels. Occasionally neoplastic cells were in endothelium-lined spaces. A few areas of necrosis and hemorrhage were seen (Figs. 2 and 3).

"Surrounding the pancreas were numerous lymph nodes, some up to 2.5 cm. in diameter, that were red-brown on cut surfaces. The lymph nodes were partly or completely replaced by neoplastic cells. The diagnosis rendered on frozen section of a portion of a lymph node was "malignant neoplasm resembling argentaffin-cell tumor." However, on fixed section, the appearance of the neoplastic cells and their arrangement led to a diagnosis of islet-cell tumor—nesidioblastoma—with metastases to regional lymph nodes.

At the time of surgery an electrophoretic pattern of the patient's serum proteins was obtained, and no abnormal component suggestive of glucagon could be discerned.

Following the operation, the 24-hour gastric drainage fell to an average of 429 ml., and examination of specimens of gastric juice revealed no free acid. The patient had a difficult postoperative course, complicated by intermittent episodes of abdominal pain which at times suggested partial obstruction. Nasogastric suction relieved these symptoms, and he was discharged on Sept. 21.

He did well for approximately three weeks, but returned on Oct. 19, with a six-day history of cramping upper abdominal pain with associated nausea and vomiting. Examination showed tenderness in the epigastrium without muscle guarding or rebound tenderness. All laboratory studies, including a serum amylase determination, were within normal limits. A scout film of the abdomen was reported to show small amounts of air in the small bowel, consistent with a diagnosis of mild reflex ileus. He was treated with intravenous fluids and nasogastric suction, resulting in the relief of symptoms, and he was discharged on Oct. 27.

His last admission was on Nov. 6, with a four-day history of severe epigastric pain radiating to the back, with associated nausea and vomiting. On this admission he appeared acutely ill, with marked epigastric tenderness and abdominal rigidity. No masses were palpable in the abdomen; bowel sounds were hypoactive. His weight was 135 lb. (61.2 kg.). Laboratory examinations were within normal limits except for a determination of serum amylase, which was reported to be 86 units. The fasting blood glucose concentration was 78 mg. per 100 ml. A diagnosis of acute pan-

Fig. 2.—Photomicrograph of the pancreatic tumor. Reduced to 69% of mag. × 100.

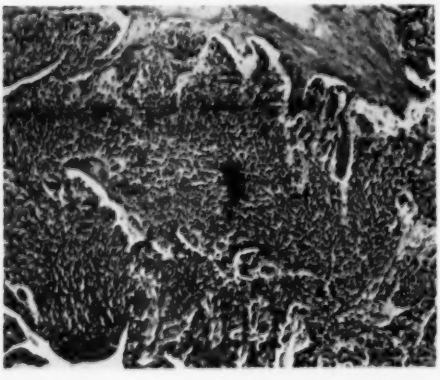
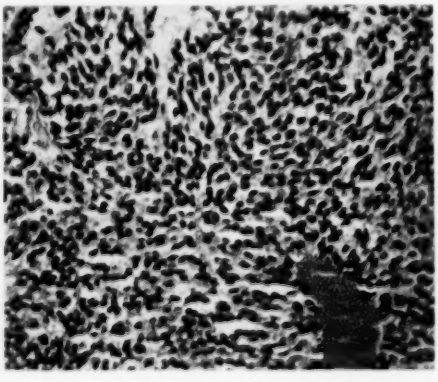


Fig. 3.— Photomicrograph of the pancreatic tumor. Reduced to 69% of mag. × 300.



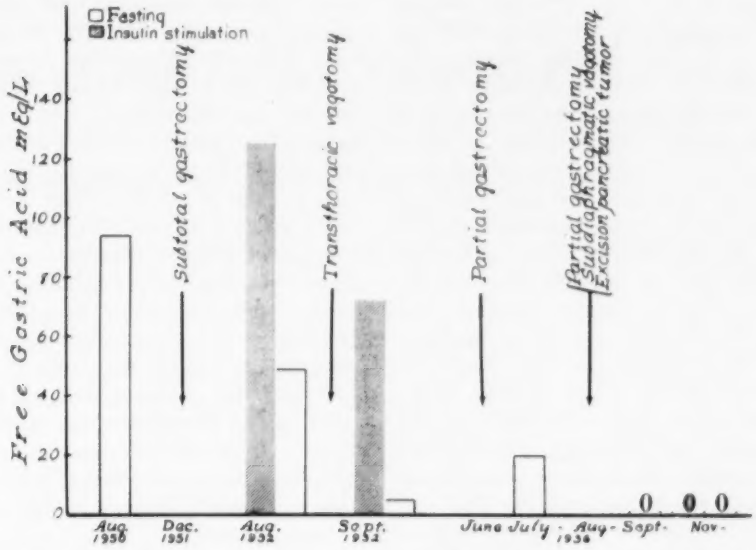


Fig. 4.—Effect of gastrectomy, vagotomy, and excision of the pancreatic tumor upon gastric acidity.

creatitis was made, and treatment consisting of gastric suction, intravenous fluids and sedation was instituted. On this regimen he became asymptomatic. After this he remained in the hospital for a few days for completion of studies relative to his ulcer problem. An electrophoretic pattern of the serum performed on Nov. 17 revealed no abnormal component. A 12-hour fasting specimen of gastric juice was 265 ml. and contained no free acid, and there was no free acid in samples of gastric juice taken after stimulation with histamine and with insulin (Fig. 4).

Comment

The association of non-insulin-producing islet-cell tumors and peptic ulceration has been reported only a few times. Ellison was able to collect 24 cases according to a recent communication, but in one-half of these cases the tumor of the pancreas was not recognized until autopsy was performed.[1] The association of these two lesions suggests the possibility that a hormone is secreted by the tumor that stimulates gastric secretion despite vagotomy and/or gastrectomy, and the effect of glucagon on gastric secretion is being investigated. Unfortunately, in most of the cases which have been reported, accurate studies of gastric secretion were not recorded, and at the present time it cannot be proved that excision of the tumor will reduce gastric secretion. In fact, Ellison suggests that one should always utilize the standard operative techniques for treatment of peptic ulceration in addition to removal of a tumor, as it is possible that unsuspected metastases in lymph nodes or nonpalpable secondary tumors elsewhere in the pancreas may continue to exert an ulcerogenic activity. The fact that approximately three-fourths of these pancreatic tumors are malignant adds to the difficulty in long-term assessment of the effect of their removal upon gastric secretion, for among the 24 patients collected by Ellison there were only 11 in whom there was treatment directed toward both the tumor and the ulcer, and only 5 of these survived longer than one year.

Although it is impossible to arrive at definitive conclusions, it is interesting to speculate upon the possible association of the pancreatic tumor and the recurrence of ulceration in the present case. The onset

of symptoms in June, 1956, was abrupt, after an asymptomatic interval of three and one-half years. Subsequently, symptoms became intractable, and the complications of perforation, hemorrhage, and obstruction all occurred within a short period. It seems unlikely that the malignant tumor had been present for three and one-half years, as there apparently was considerable growth between the operation in June and the one in August. At the time of resection the tumor was large and nodal metastases were obvious, whereas the surgeon was unable to identify the tumor in June. These findings, plus the persistence of free acid in fasting specimens tested prior to resection of the tumor, might suggest a relationship between the two lesions; however, in view of the fact that a third gastrectomy and a subdiaphragmatic vagotomy were performed simultaneously with removal of the tumor, it is not possible in this case to state with accuracy which procedure was responsible for the postoperative achlorhydria.

We have reviewed the problem of marginal ulcer in our hospital and have reexamined the pancreas of all patients (4) dying in this hospital who had marginal ulcer at the time of death or who had been treated for recurrent ulceration in the past. None of these had a pancreatic tumor. Furthermore, since the original report by Zollinger and Ellison, we have carefully explored the pancreas each time surgical treatment for marginal ulcer has been instituted, and the case here reported is the only one in which a tumor of the pancreas has been encountered. Consequently, it would appear that the association of these two lesions is quite rare; and at the present time the available data do not allow any definite conclusion concerning their relationship. It is unlikely that definitive data can be obtained on this subject except by a collection of cases from numerous medical centers, and it is to be recommended that all similar cases be reported in detail in order to aid in this evaluation.

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Cardiac Arrest One Hour Following Pneumonectomy

Successful Resuscitation and Religation of Right Pulmonary Artery

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Introduction

This report records the successful resuscitation of a patient who had a cardiac arrest in the postoperative room one hour following the completion of a right pneumonectomy for pulmonary tuberculosis at Olive View Sanatorium, on Nov. 11, 1954. The patient had sudden cessation of all vital signs due to a massive hemorrhage from the right main pulmonary artery and was considered dead. The availability of trained personnel and proper facilities made immediate religation of the pulmonary artery and cardiac resuscitation possible. The patient left the hospital with no neurologic sequelae.

Cardiac resuscitation after ventricular fibrillation or cardiac arrest occurring in the operating room is now a well-established procedure, which has been successfully performed on many occasions. In at least two instances successful resuscitation of a patient suffering from ventricular fibrillation outside the operating room has been reported.[2-4] We have been unable to find a similar report of the recovery of a patient who had a cardiac arrest and was apparently dead from massive postoperative hemorrhage outside the operating room.

Report of Case

A 50-year-old white male was admitted to Olive View Sanatorium on Aug. 15, 1952. He had contracted tuberculosis early in 1950 and had received sporadic care at home over a two-year period. During this time the tuberculosis process had become far advanced, with bilateral cavitation seen on x-ray (Fig. 1), and the patient had a persistently positive sputum. On examination he was weak and debilitated, with signs of bilateral cavitation. He was placed on treatment with dihydrostreptomycin sulfate U. S. P., 1 gm. twice weekly, and aminosalicylic acid, U. S. P., 16 gm. four times weekly, upon admission to the hospital. In May, 1953, because of a persistently positive sputum, isoniazid U. S. P., 150 mg. daily, was added to the regimen. Serial x-ray studies showed disappearance of the cavity on the left side. A 6 cm. cavity persisted in the right midlung field with considerable diffuse nodular disease (Fig. 2). His sputum remained positive on concentrate, but his general condition had markedly improved and he had gained 30 lb. in weight. The vital capacity was 2800 cc.; the breath-holding time was 31 seconds, and he could walk 300 ft. without dyspnea. At surgical conference in October, 1954, it was evident that maximum improvement had been made on the 26-month bed rest and chemotherapy. Because of the persisting cavitation in the right midlung field, the positive sputum, and the diffuse nodular disease, a right pneumonectomy was recommended.

On Nov. 9, 1954, a right pneumonectomy was performed. The thoracic cavity was opened through a posterolateral approach through the fifth rib bed. The pleura was markedly thickened, and the lung was dissected free in both the intra- and the extrapleural plane. Extensive nodular disease was noted throughout the entire lung in addition to the cavity near the right hilus. The pulmonary vessels were secured by individual ligation technique. Some difficulty was encountered, due to the short length of the main pulmonary artery. A No. 2 and a second, 00, single silk suture were used as ligatures. The divided bronchus was closed with interrupted fine silk sutures. A pericardial fat graft was placed on the bronchial stump and the chest wall closed in layers. The procedure was completed in three hours. After adjustment of the intrapleural pressure to a slightly negative level, the patient was returned to the postoperative room, in excellent condition with stable vital signs. The blood pressure at the beginning of the operation was 115/75, and at the completion it was 105/75. There was no abnormal blood loss during surgery, and he was given 1500 cc. of citrated whole human blood U. S. P. during the operative procedure.

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From the Surgical Services of Olive View Sanatorium.

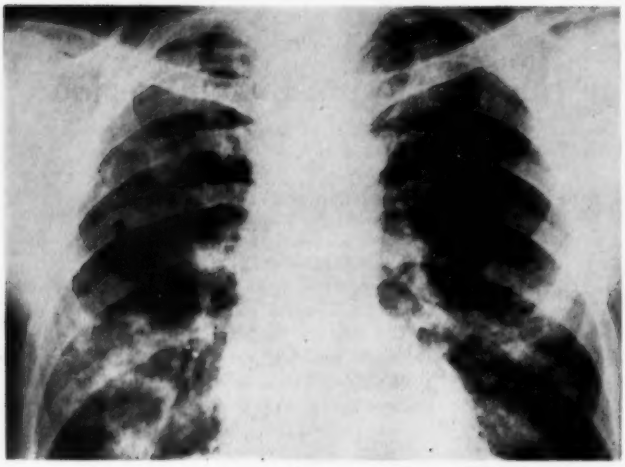

Fig. 1.—The chest roentgenogram shows multiple bilateral cavitation on admission to Olive View Sanatorium.

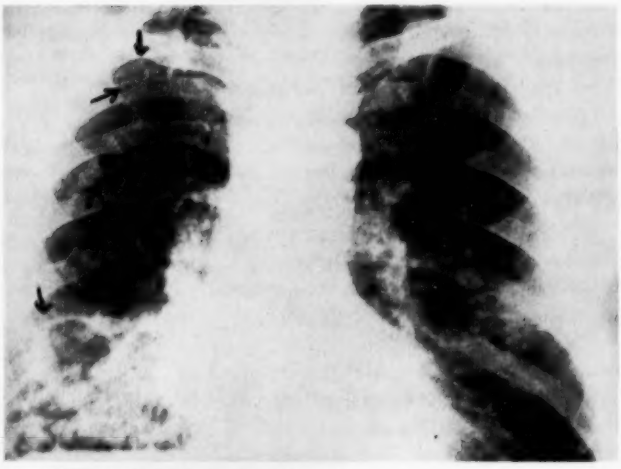

Fig. 2.—After intensive antimicrobial therapy the preoperative film shows that the left lung has cleared considerably, although cavitation persists in all lobes of the right lung.

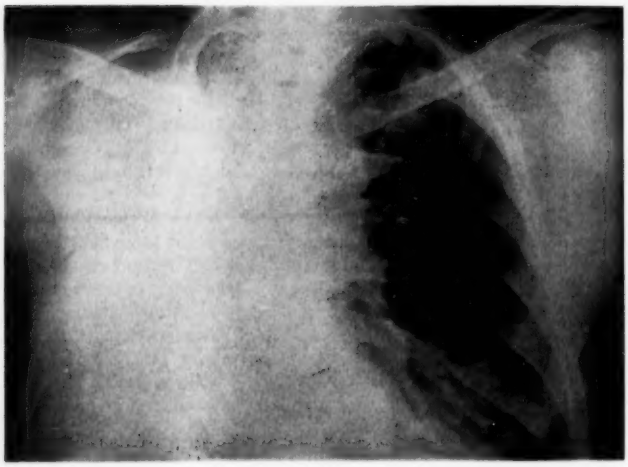

Fig. 3.—Seven months after the pneumonectomy, no active tuberculous disease is seen in the left lung field. A postpneumonectomy thoracoplasty has been performed on the right side.

Approximately one hour after the surgery had been completed, the special nurse hurriedly reported that the patient had died. There were no respirations, pulse, or audible heart beat. The blood pressure was zero, and the entire right chest was dull to percussion.

The patient was returned immediately to the operating room, which was being prepared for another thoracotomy. The anesthetist immediately inserted an intratracheal tube for the insufflation of oxygen. Without stopping for aseptic technique, the chest was hurriedly reopened. Large quantities of Type O blood were administered through a cannula in the left lesser saphenous vein, which had been kept patent following surgery. The right hemithorax was found to be almost completely filled with blood, and the main pulmonary artery was widely open, apparently due to cutting through of the proximal ligature. There was no cardiac movement. The stump of the right pulmonary artery was quickly sutured with a running 00000 arterial suture. While this suture was being completed, the heart began to beat, and soon the cardiac contractions became strong. The pulmonary artery appeared to be well secured, and the chest wall was rapidly closed. The patient began to react before the chest wall was closed. It was estimated that the opening of the chest took approximately 3 minutes, and a total of 30 minutes were included in the securing of the pulmonary artery and the chest-wall closure. During this procedure approximately 2500 cc. of blood was administered. The blood pressure was 80/50 at the completion of the second operation. The postoperative course from then on was entirely uneventful. On Feb. 3, 1955, a right tailoring thoracoplasty was performed in order to prevent excessive mediastinal shift and possible reactivation of the latent disease of the left lung. He was discharged on Aug. 16, 1955, with stable disease, as evidenced by the x-ray (Fig. 3). He has remained well to the present time.

Comment

Massive postoperative hemorrhage from a major pulmonary vessel occurring after the patient has been removed to his room is usually a catastrophic and rapidly fatal event, due to the exsanguination. Postoperative intrapleural bleeding, which is less severe and more chronic in nature, usually occurs from intercostal and bronchial vessels. The hemorrhage most frequently can be handled satisfactory by conservative measures and is seen in 2% to 5% of cases undergoing pulmonary resection for tuberculosis. Deliberate surgical intervention may be necessary in certain instances. Analysis of a series of 500 consecutive pulmonary resections which have been performed at the Olive View Sanatorium in the last three years revealed 9 cases in which postoperative intrapleural hemorrhage was serious enough to necessitate thoracotomy within 36 hours following the original surgery (1.8%). Of these cases, five were due to uncontrolled bleeding from the bronchial vessels, and in four there was oozing from the branches of the intercostal vessels. In each case the postoperative hemorrhage was successfully managed at the second thoracotomy.

Actually, the number of cases in which death has ocurred from the reopening of a main pulmonary artery is not known. When the surgery has been performed carefully, this complication usually occurs as the result of the ligature cutting through a diseased pulmonary artery. Of course, ligatures may slip off when they are not securely applied. Recently we had a ligature cut through a diseased pulmonary artery following a pneumonectomy just before the chest was closed. By opening the pericardium and clamping the artery, it was possible to repair it securely.

The successful outcome of the present case is due to a number of factors. The prompt detection by the special nurse of the cessation of vital signs and the immediate decision to reopen the chest were of major importance. The readiness of the operating room for a thoracotomy and the immediate availability of the anesthetist made the performance of the thoracotomy almost instantaneously possible once the decision was made. The location of the postoperative room next to the operating room further cut down the delay. This consideration is a strong argument for keeping the patient in a postoperative recovery room close to the operating room and not moving him to a distant ward. The availability of a large quanity of Type O blood and the presence of a cannula in the ankle vein made rapid restoration of the blood volume

possible. Plasma expanders may have been effectual, but there is no question that whole blood, with the oxygen-carrying capacity of the hemoglobin, offers the best medium to provide oxygen to the sensitive nervous system. Since no neurologic sequelae of any kind were noted, it must be presumed that some cerebral circulation was maintained for a portion of the time that intervened from the moment the diagnosis of cardiac standstill was made until the heart action was resumed. We believe it is important that the patient had no prolonged periods of hypoxia during the operation or in the immediate postoperative period, so that the brain was well oxygenated up to the point of the cardiac standstill.

There are certain lessons to be learned by the study of this case. The most important is that of prevention of hemorrhage from a divided main pulmonary artery. If there is not sufficient length of pulmonary artery to provide for two ligatures with an intervening "bead," two techniques are applicable: 1. The application of a proximal noncrushing arterial clamp permits the closure of the vessel with a running arterial suture, much as one would secure the divided end of a ductus arteriosus. (This was the technique used in our case at the second operation, herein reported.) 2. Opening the pericardium offers exposure of additional length of pulmonary artery for ligation.[1] A band of nonirritating cellophane may be placed around a friable pulmonary artery to prevent the ligature from cutting through. Any of these methods is satisfactory, and the actual technique used must depend on the judgment and previous experience of the surgeon in handling such a situation. Opening the pericardium is not a dangerous procedure, as was formerly believed. We have employed it whenever it was necessary to adequately expose and secure the pulmonary artery. However, if the pericardium is opened, we believe that a small window in the pericardium should be left near the apex of the heart to drain dependently all fluid developing from a possible traumatic pericarditis and thus prevent cardiac tamponade.[3]

As long as operations are performed, there remains the possibility of severe hemorrhage from a major artery in the early postoperative period. Therefore the surgeon must always be prepared to deal with this eventuality. The importance of the immediate diagnosis of cardiac standstill cannot be stressed too much. This can be made only by carefully trained personnel, preferably in a recovery room or postoperative room where specially instructed nurses and doctors are available. This postoperative room should be very close to the operating room. Ideally, a resuscitation team should be instantly available. This includes a surgeon, an anesthetist, and a nurse, all of whom have been schooled in their special tasks. Emergency equipment should be ready always and should include a thoracotomy set, adequate anesthetic apparatus, matched blood ready for transfusion, and reserve Type O blood and/or plasma and plasma expanders. The cannula or large-bore needle is left in the patient's vein until the patient has properly recovered from the operation and the dangers of immediate hemorrhage have passed.

Summary

An instance of successful resuscitation of a patient with cardiac arrest due to massive intrapleural hemorrhage is reported, in whom the right main pulmonary artery was religated and the heart revived one hour after pneumonectomy. Various technical steps which should minimize the occurrence of massive hemorrhage are reviewed. However, when proper facilities are available, cardiac arrest in the postoperative period due to exsanguinating hemorrhage, even from a major pulmonary vessel, is not necessarily fatal.

This case gives hope for the future successful management of what is usually a fatal complication in the recovery room and is a stimulus for every surgical service to review constantly their emergency set-up

in order to be ever prepared for the adequate treatment of such massive hemorrhage.

2010 Wilshire Blvd. (57) (Dr. Brewer).

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Malignant Brenner Tumor

MARGARET MACKINNON, M.D., and MALCOLM B. DOCKERTY, M.D., Rochester, Minn.

The malignant Brenner tumor is an unusually rare lesion, and thus far only six cases have been reported in the literature. Forty-two cases of Brenner tumor were reported from the Mayo Clinic in 1950, all of which were benign.[1] However, a malignant Brenner tumor was seen in 1954. A report of this case is presented herewith.

Report of Case

A 59-year-old white woman (sextigravida, quadripara, two abortions) was first seen at the Clinic in 1938 because of symptoms referable to a duodenal ulcer. Pelvic examination at this time revealed a leiomyoma in the uterus 3 to 4 cm. in diameter.

In 1954 the patient returned, complaining of lower abdominal enlargement of two weeks' duration. She reported that the menopause had occurred in 1947. On examination a firm, somewhat nodular mass was found in the left adnexal region. Abdominal hysterectomy and bilateral salpingo-oophorectomy were carried out.

The uterus was not remarkable except for the presence of a small adenomatous polyp and an intramural fibromyoma 2 cm. in diameter. The tubes appeared normal and the right ovary atrophic. The left ovary was the seat of a lobulated, encapsulated, partly solid, and partly cystic tumor, measuring 20 by 15 by 12 cm. and weighing 1900 gm. The tumor was removed, and on bisection a large amount of fluid escaped from a uniocular cystic compartment, which occupied the bulk of the mass. The mass, after collapse, was estimated to measure about 14 cm. in diameter. The remaining portion (Fig. 1) was solid, lobulated, white, firm, and gritty, similar in color and texture to a fibroma. However, those portions of the solid component which lined the interior of the cyst were definitely of different composition, being shaggy, somewhat friable, soft, and brownish-gray.

Microscopic examination of sections of the solid whitish portion of the tumor showed structures typical of Brenner tumor (Fig. 2*A*). Islands of squamous-like cells, often with cystic, columnar-

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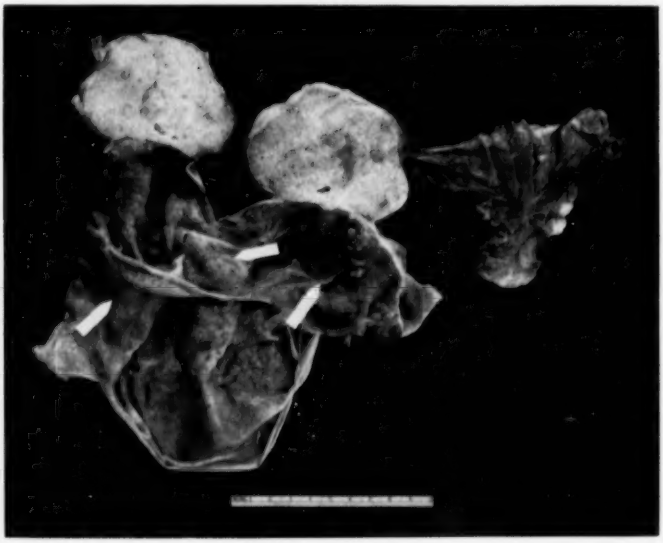

Fig. 1.—Gross tumor, showing solid and cystic components. Villous aspects are apparent at the junction of the two.

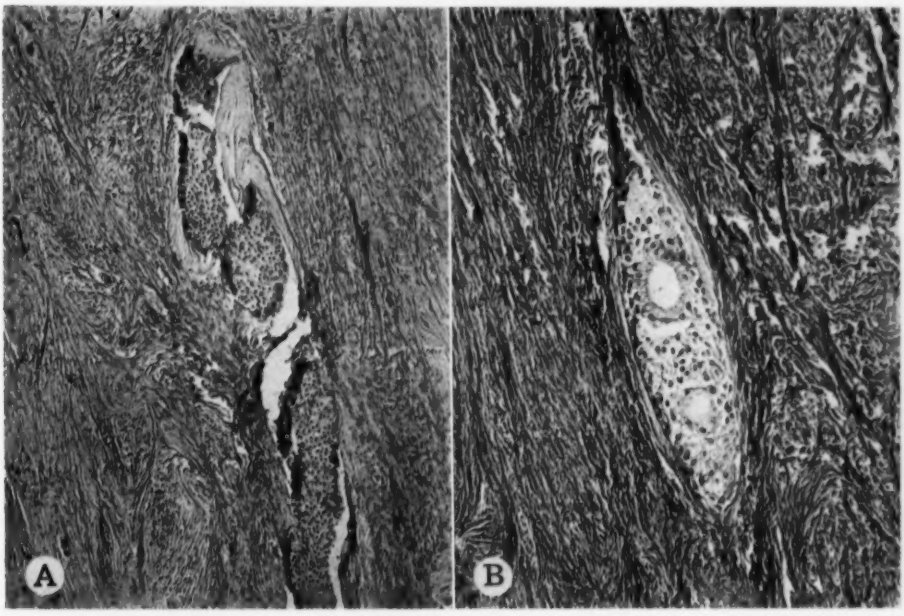

Fig. 2.—*A*, section through dense aspect of solid portion, showing benign Brenner tumor with epithelial island lying in a fibromal-like matrix. Hematoxylin and eosin; × 75. *B*, another island of benign epithelium, showing central cavities lined by columnar, mucus-producing cells. Hematoxylin and eosin; reduced to 97% of mag. × 150.

lined centers and containing mucus (Fig. 2*B*) were embedded in a fibrous and hyaline matrix with scattered areas of calcification. Near the inner surface of the solid component the fibrous stroma gradually decreased as a result of epithelial overgrowth until, adjacent to the frond-like structures observed grossly, it was represented by tenuous strands only. These strands served as the vessel-carrying cores for the villous papillary folds of epithelium now piled from 8 to 15 layers thick in proliferating mantles (Fig. 3*A* and *B*). Through the high-power objective the epithelium here, in contrast to its completely benign appearance in the aforementioned solid areas, exhibited large, hyperchromatic nuclei, large nucleoli, and one or two mitotic figures in each field (Fig. 3*C*). Giant epithelial forms were noted occasionally. Transitions between this malignant-appearing epithelium and its benign counterpart in the regions of typical Brenner tumor were easily identified.

The peritoneum was not involved, the entire malignant process being limited to that particular portion of the cyst which bore contact with the solid component of the tumor.

Comment

The ovarian Brenner tumor is a neoplasm which must be distinguished grossly from the fibroma and thecoma. It appears in solid, cystic, and mixed forms, and the two last-named may be mucinous. Microscopically, nests of epithelial cells are distributed in fibromatous connective tissue. The epithelial cells are squamous-like but lack keratohyaline granules and intercellular bridges.

In 1907 Brenner [2] described three such tumors under the designation "oophoroma folliculare." In 1935 Bland and Goldstein [3] reviewed the available literature regarding Brenner tumor. Of the 60 patients whose cases were reported, 6 died within one year after operation; 1 patient died of "metastasis."

In 1945, von Numers [4] published reports of two cases of malignant Brenner tumor. A brief review of each case follows.

Case 1.—A 50-year-old woman, tripara, had back pain of several years' duration, abdominal pain for six months, and abdominal fullness for several weeks. At operation bilateral ovarian tumors were found. The right ovary was enlarged to fist-size and contained a pseudomucinous

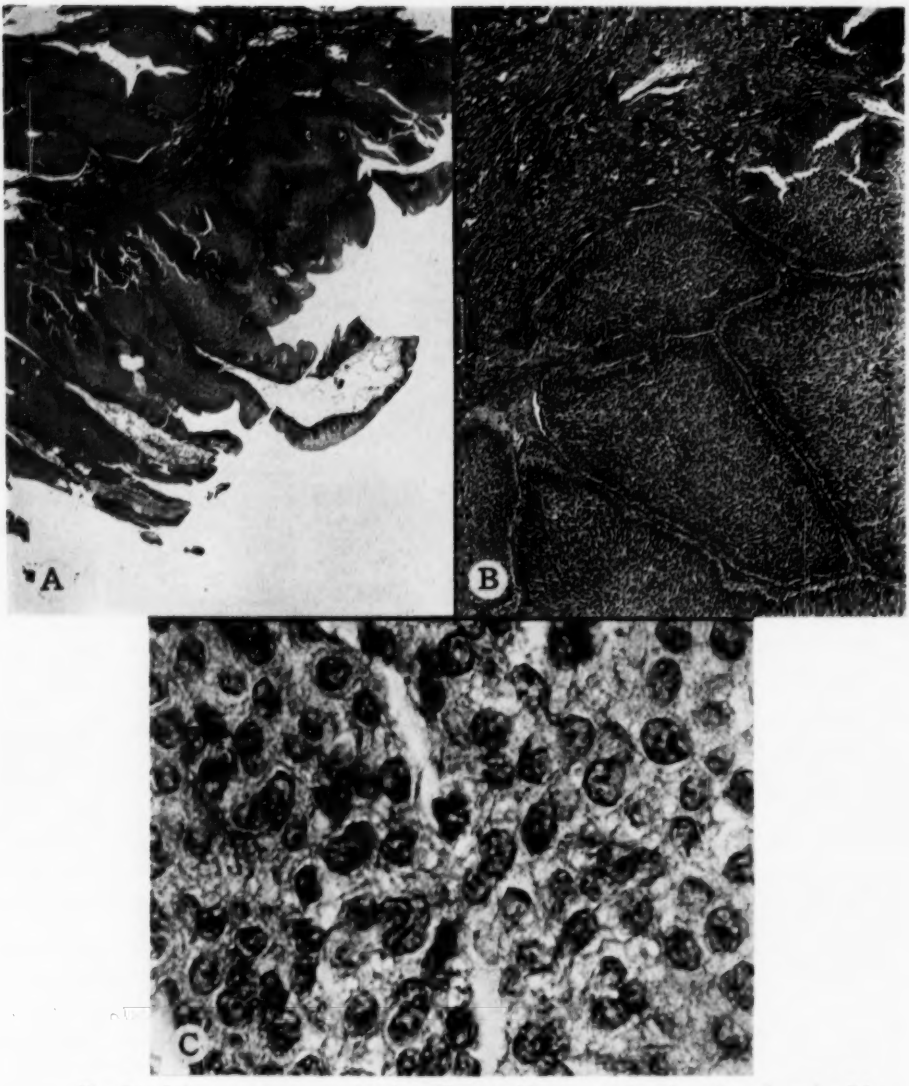

Fig. 3.—*A*, low-power aspect, showing villous architecture at junction of cystic and solid portions of tumor. This villous aspect has been noted previously in malignant Brenner tumors. Hematoxylin and eosin; × 10. *B*, tenuous character of the connective-tissue stalks supporting the epithelial cells of the villi. The epithelial cells are quite dark-staining, and an occasional giant cell can be seen. Hematoxylin and eosin; × 100. *C*, section from a villous region. The pleomorphism and mitotic activity of the epithelial cells are apparent. Hematoxylin and eosin; reduced to 97% of mag. × 850.

cystadenoma. The left ovary was partially solid and partially cystic, and was enlarged to the size of a woman's head. The solid portion consisted of malignant Brenner tumor, with epithelial pleomorphism, and pathologic mitotic figures. Numerous metastatic growths were found in the pelvic peritoneum. The patient received irradiation after total hysterectomy and bilateral salpingo-oophorectomy. The tumor recurred, and formation of ascites ensued. The patient died one year after operation.

Case 2.—A 57-year-old woman, tripara, had had a lump in the lower part of her abdomen for 12 years. Two months prior to her admission to

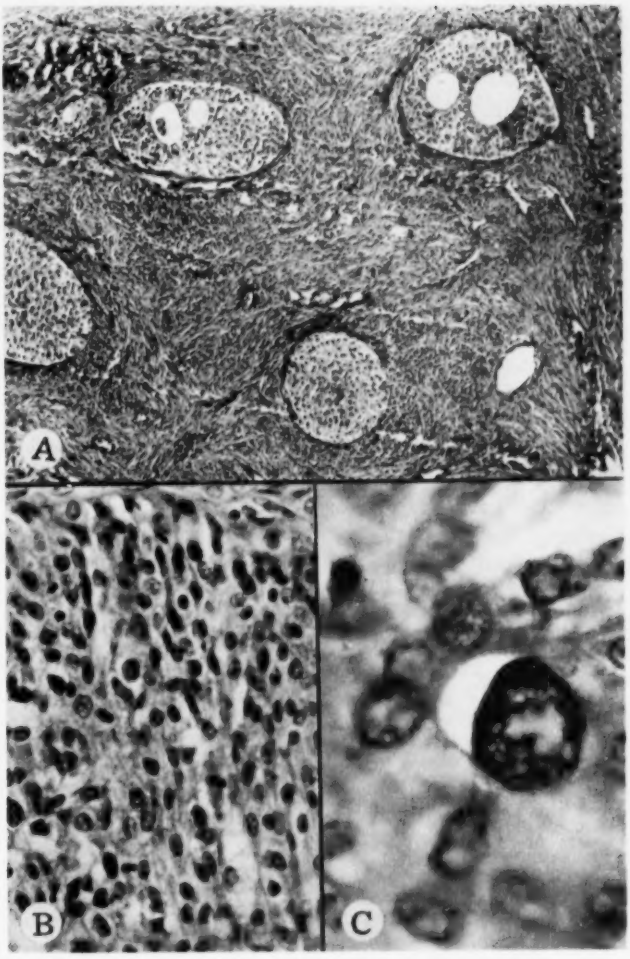

Fig. 4.—*A*, benign region from malignant Brenner tumor. Note the typical islands of pale-staining polygonal cells. The central cystic cavities contained mucus. Hematoxylin and eosin; × 70. *B*, section from another zone, depicting increased cellularity, nuclear hyperchromatism, and mitotic spindles. Hematoxylin and eosin; × 398. *C*, section from a still more pleomorphic area of the same tumor. Note the malignant giant cell. Hematoxylin and eosin; × 1000. Courtesy of Dr. S. H. Colvin, of Baton Rouge, La.

the hospital the lump increased in size and became painful. At operation, the right ovary was found to be enlarged to one and a half times the size of a man's head and consisted of a pseudomucinous cystadenoma, with a solid portion consisting of a malignant Brenner tumor. The patient died about one year after operation. Necropsy was not performed.

Dubrauszky and associates reported a case of malignant Brenner tumor in 1947 [5] and another in 1949.[6] The first patient was a 70-year-old woman who had undergone laparotomy. After 3000 ml. of ascitic fluid had been withdrawn, a left ovarian tumor, 13×15×17 cm., was discovered and removed. Microscopic investigation showed it to be a Brenner tumor with cystic formation. Carcinomatous portions were noted microscopically in both solid and cystic portions. At currettage, endometrial hyperplasia also was noted.

The second patient was a 69-year-old woman, quintipara, who was first seen because of a mass in the lower abdominal region and loss of weight. She had had a mastectomy nine years previously for carcinoma. At operation, a left ovarian tumor, measuring 9×10×16 cm., was removed. The tumor was partially solid and partially cystic, with pseudomucinous portions. Marked atypical changes with mitotic figures

and giant cells seen in the epithelial portions of the Brenner tumor indicated its malignant nature.

Novak recently reported a case of malignant Brenner tumor seen by Limburg.[7]

Rawson and Helman[8] reported the case of a 70-year-old woman who was operated on for an abdominal mass. A tumor was found invading the broad ligament and the lateral pelvic wall. It was impossible to dissect out all the neoplastic tissue. Deep x-ray therapy was initiated on the seventh postoperative day. Vaginal bleeding began five months after operation, and the patient died five and one-half months later. Necropsy showed involvement of the posterior wall of the bladder and lateral extension with invasion and obstruction of the left ureter and compression of the right ureter. The vaginal and rectal walls were invaded, and the kidneys also were involved.

Through the courtesy of Dr. S. H. Colvin,[9] of Baton Rouge, we have had the opportunity of reviewing slides from still another malignant Brenner tumor (Fig. 4*A*, *B*, and *C*).

Summary

Malignant Brenner tumor is a very rare entity. A review of the literature discloses only six cases. A seventh case, encountered recently at the Mayo Clinic, is reported, and photomicrographs of an eighth case are presented.

The Mayo Clinic.

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Purulent Pericardial Effusion Treated by Incision and Drainage

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The presence of a subacute or chronic pericarditis with effusion is not a common condition encountered on a surgical service. The surgeon is much more aware of acute pericardial tamponade secondary to penetrating wounds of the heart. Here the condition can easily be suspected by the site and type of injury, as well as the dramatic clinical picture and fairly typical signs.[1,2] A small effusion into the pericardial sac may be quickly fatal, since there is little dilatation of the pericardium and shock can occur quickly. Elkin and Campbell[3] have reported a case in which 5 cc. of blood in the pericardium has given a 0/0 arterial blood pressure. Subacute or chronic pericarditis, on the other hand, can lead to massive effusion without the striking clinical picture of acute tamponade. Yu et al.[8] have reported a case in which pericardial aspiration yielded 1910 cc. of fluid on one occasion. The most outstanding symptom is dyspnea in most of these patients. This symptom, however, as well as most of the physical signs, is also easily confused with the symptoms of myocardial infarction, acute or chronic pulmonary disease, and cardiac failure. Williams and Soutter,[7] in a thorough review of pericardial tamponade, have pointed out some of the misconceptions in physical signs, as well as the importance of a pulsus paradoxus and pulsating neck veins, which are often missed. Goyette[4] has emphasized the presence of a pericardial friction rub in the first 36 hours as an important sign of differentiation from acute myocardial infarction. Needless to say, the diagnosis is most difficult unless kept in mind by the observer of the patient. It is our purpose to report such a case and the dramatic response to adequate surgical therapy.

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Report of Case

A 56-year-old man was admitted to Bellevue Hospital for the second time on March 23, 1956. The patient was confused and could only state by way of history that he had been feeling "sick" for over a week, with a nonproductive cough and mild shortness of breath the day prior to admission. His previous hospitalization, in November, 1952, was initiated by complaints of periumbilical pain and weight loss, for which no definitive diagnosis was reached despite thorough investigation.

Physical examination, on March 23, gave an impression of both acute and chronic disease. The patient was cyanotic, with brownish pigmentation of the exposed areas of the skin. There was no pigmentation of the buccal mucosa. The extremities were cool but not clammy. There was evidence of marked dehydration. Blood pressure was unobtainable; pulse rate, 112; respiratory rate, 28, and rectal temperature, 98.0 F. Examination of the lung revealed loud, moist inspiratory and expiratory rales at the left lateral field and left base posteriorly. The heart sounds were normal in quality and rhythm. The heart size was judged by percussion to be enlarged to approximately 2 cm. past the midclavicular line. The abdominal examination was negative. There was no peripheral edema or clubbing.

The initial total leukocyte count was 28,000 per cubic millimeter, with 80% polymorphonuclear cells, 17% segmental cells, and 3% lymphocytes. Hemoglobin was 18.5 gm. per and hematocrit 53%. Urinalysis was unremarkable except for a specific gravity of 1.013. A bedside chest plate was technically unsatisfactory but did reveal a density in the left lower lung field suggestive of a pneumonic infiltration. A blood culture was taken which proved to be sterile.

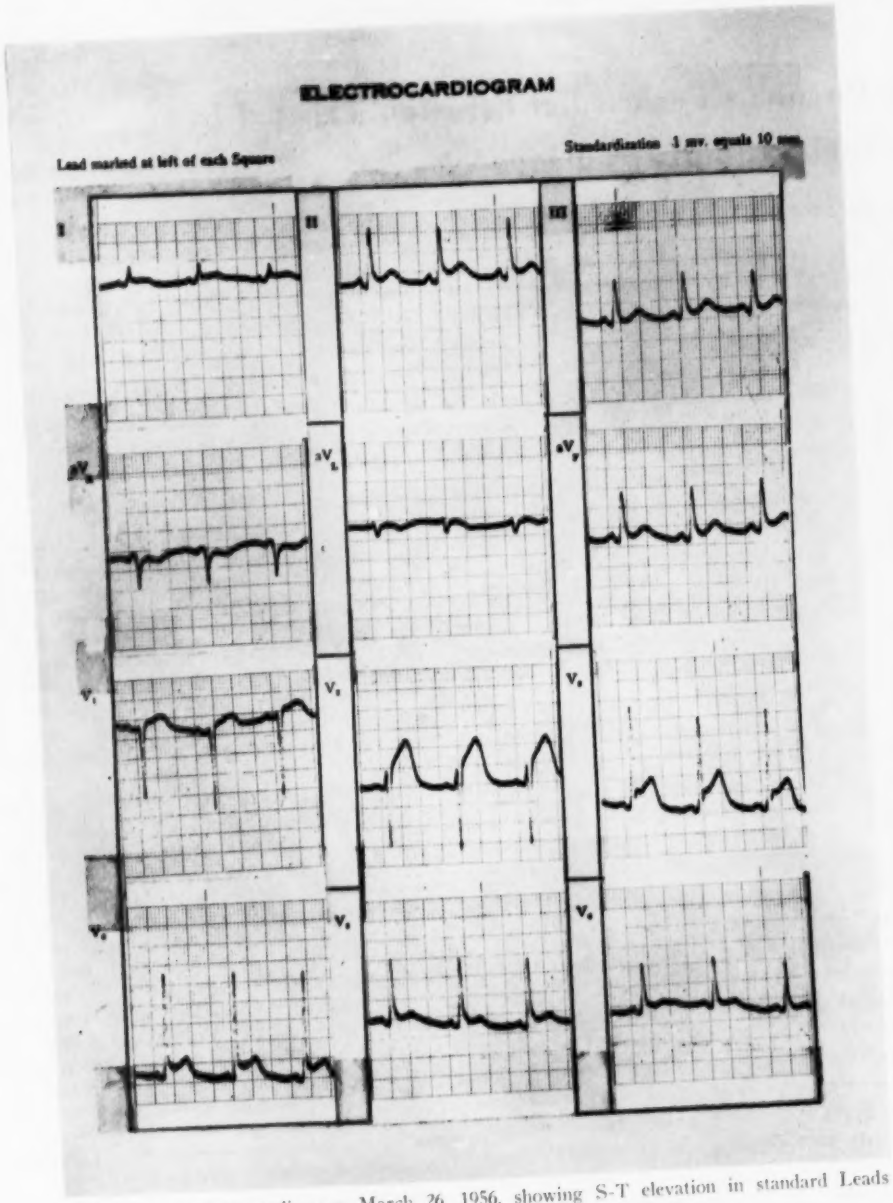


Fig. 1A.—Electrocardiogram March 26, 1956, showing S-T elevation in standard Leads I, II, III_F, aV, and V_1-V_6.

The initial diagnostic impression was that of left lower lobe pneumonia with overwhelming septicemia and shock. The patient was placed on continuous intravenous fluids, including 5,000,000 units of aqueous penicillin, as well as 2 gm. of streptomycin intramuscularly per day. A slow levarterenol bitartrate intravenous "drip," 4γ per milliliter, was instituted in order to maintain a systolic blood pressure of 100. Oxygen was administered via BLB mask.

On March 24, after 24 hours of treatment, the clinical picture was unaltered. The temperature was still normal. The hemoglobin had dropped to 15.5 gm. per 100 cc., most probably on the basis

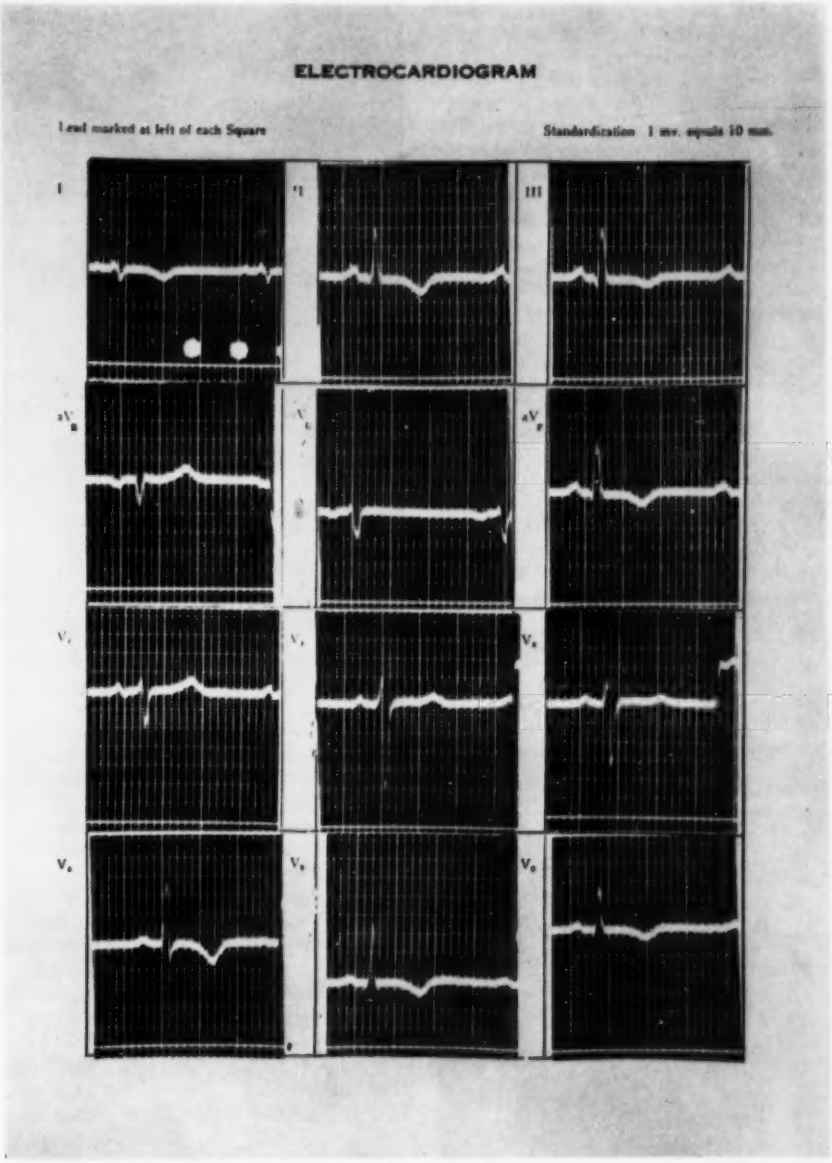


Fig. 1B.—Electrocardiogram April 4, nine days after initial tracing, now shows that the S-T segment has returned to the base line with prominent T-wave inversion appearing in standard Leads I, II, III, aVF, and V5-V6.

of hydration. Levarterenol "drip" was still required to maintain blood pressure. At this juncture it was decided to institute corticoid therapy in the form of intravenous hydrocortisone alcohol, 100 mg., at the same time, administering cortisone acetate intramuscularly, 50 mg. every six hours. This was done on the basis of severe infection unresponsive to 24 hours of conservative therapy,[8] as well as the wholely clinical suggestion that the underlying process may have represented adrenal insufficiency which was precipitated into crisis by intercurrent infection.

On March 26 the patient was somewhat more alert and it was possible to discontinue the levarterenol. The temperature still was not elevated. Hemoglobin was now down to 14.5 gm. per 100 cc., where it remained throughout the hospital course. Total leukocyte count was 17,750, with 18% segmental cells and 80% polymorphonuclear cells. Blood urea nitrogen was 77 mg. per 100 cc. However, urine output continued good, and in two days the urea nitrogen level had dropped to 27 mg. per 100 cc. Electrolytes were normal other than a value of 3.3 mEq. per liter for the potassium determination.

The electrocardiogram (Fig. 1A) showed S-T wave elevations without either significant Q waves or reciprocal S-T depression. These findings, in short, gave the first clue to the diagnosis of pericarditis.

By March 28 the patient had continued to show slight improvement. He was able to take fluids by mouth and sit up in bed. He did not complain of any pain or particular discomfort other than minimal dyspnea. Penicillin and streptomycin were continued intramusclarly, and cortisone was given in decreasing amounts for the last day, along with corticotropin preparatory to discontinuance. The chest plate in the erect position now definitely demonstrated the left lung infiltration, as well as an enlarged heart. The cardiac shape at this time was not thought to be specific as to diagnosis.

Fig. 2.—PA chest plate taken on March 31, prior to pericardial aspiration.

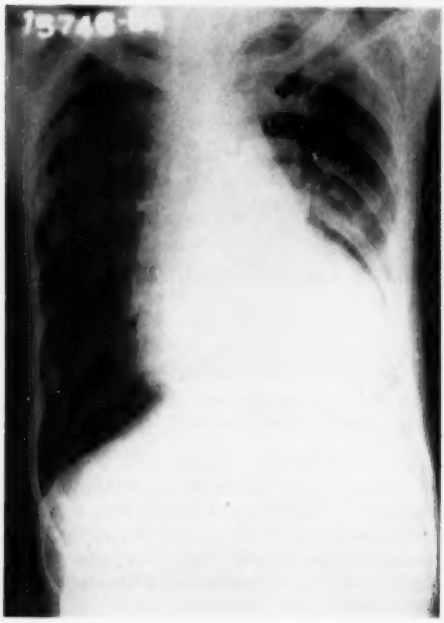


Fig. 3.—Lateral chest film showing air in pericardial cavity.

On March 30 the temperature was elevated to 100 F. For the first time, a pulsus paradoxus of over 15 mm. Hg. was noted. Blood pressure was 115/70. Over the left lung base moist rales were heard, as before. The right lung was clear. The heart sounds were perfectly normal in quality and intensity. There was no friction rub.

On March 31 the patient was somewhat more lethargic. The neck veins were distended at 30 degrees and pulsatile. Venous pressure measured 145 mm. of water in the right median basilic vein and rose to 170 mm. with right upper quadrant pressure. No pulsations of the heart were noted on fluoroscopic examination.

A chest plate taken at this time (Fig. 2) seemed more characteristic of pericardial tamponade in view of the sharp diaphragmatic cardiac angle, as well as the clear lung fields on the right, in contrast with the raised venous pressure and enlarged heart.

Pericardial paracentesis was performed through the left xiphisternal angle, and 300 cc. of purulent, creamy-white fluid was removed. Venous pressure dropped to 80 mm. after the procedure with no change in arterial pressure. Two million units of aqueous penicillin and 1 gm. of streptomycin, as well as 20 cc. of air, were injected locally (Fig. 3).

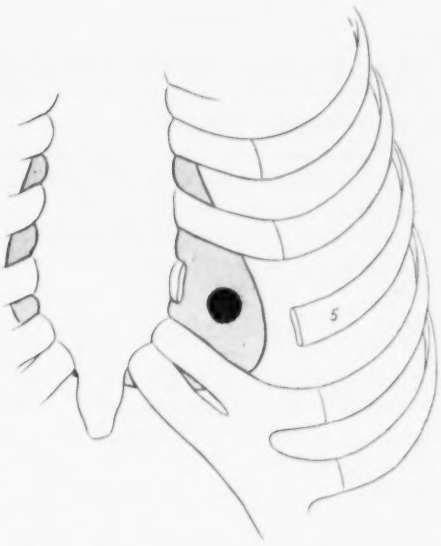


Fig. 4.—Diagrammatic sketch showing site of removal of pericardial "button" beneath resected fifth costal cartilage.

A smear of the pericardial aspirate revealed myriads of polymorphonuclear cells but no organisms. Routine cultures and cultures for acid-fast studies subsequently were reported as sterile.

It was decided, at this point, to carry out incision and drainage of the pericardial cavity as an emergency procedure. With the patient under endotracheal anesthesia, an incision was made over the left fifth costal cartilage. After division of the perichondrium, the costal cartilage was resected intact. The internal mammary vessels were divided and ligated. This gave access to the anterior mediastinum directly over the pericardium to the right of the pleural reflection (Fig. 4). The incision was carried down to the epicardial fat, and after two traction sutures were placed on either side, the thickened pericardium was opened. Pus immediately exuded, and 450 cc. more was aspirated. A 2 cm. portion of the pericardium was taken for biopsy. At no time was the plural cavity entered. The wound was partially closed, leaving the defect in the pericardium for the insertion of three Penrose drains. The patient withstood the procedure well.

Cultures taken of the pericardial exudate at surgery were again negative. Biopsy section of the pericardium on microscopic examination showed thick fibropurulent exudate.

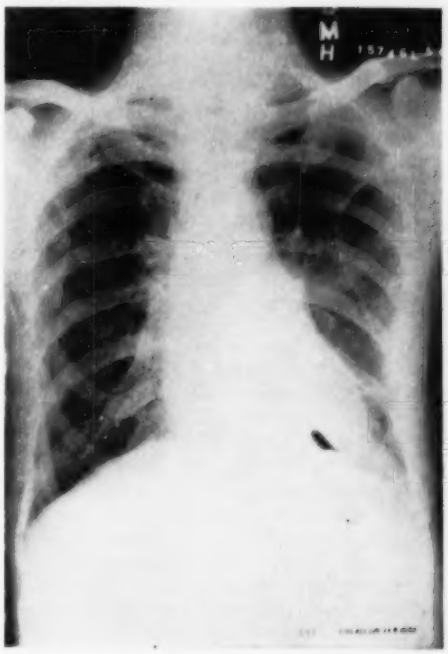
Postoperatively, the patient did well until the second week, when there occurred a hypotensive episode, which required levarterenol intermittently for two days. The heart size decreased, and there was slow resolution of the pneumonic process. The chest wound drained extensively for the first postoperative week and by the third week was healed. Postsurgery urinary 17-ketosteroid and 17-hydroxysteroid determinations were normal, as was the response to an eight-hour corticotropin infusion, thus excluding the likelihood of adrenal insufficiency.

When discharged on June 11, on the 73d postoperative day, the patient was ambulatory without dyspnea. The heart size was normal, as was the pulsatile activity under fluoroscopic examination (Fig. 5). He has been lost to further follow-up.

Comment

This represents a case of purulent pericarditis with massive effusion which was relieved by surgical decompression. No one sign or symptom alone was pathognomonic of this complication of the pneumonia. The electrocardiogram directed attention to the possible establishment of pericarditis, and a pulsus paradoxus aided in enhancing this suspicion. Pericardial aspiration of 300 cc.

Fig. 5.—Final chest plate taken 72 days after surgery.



of a purulent fluid definitely confirmed the diagnosis.

Surgical decompression by removal of a wedge of pericardium allowed direct drainage of the effusion, as well as providing a specimen for pathological examination. Repeated aspirations of the pericardial cavity carried with it the danger of cardiac arrhythmias, laceration of the heart or coronary arteries, pneumothorax, and syncope. Williams and Soutter [7] and Proudfit and Effler [6] have reported the creation of a pleuropericardial "window" for drainage in some of these cases. With the use of antibiotics, it would seem that a direct attack on the removal of pericardium alone is a simpler procedure and avoids possible contamination of the pleural cavity. Postoperatively drainage was adequate and secondary infection of the pericardium did not occur. The chest wound was well healed in three weeks.

Etiology was not definitely established, since routine cultures and cultures for acid-fast organisms were negative and biopsy of the pericardium revealed only acute inflammatory tissue with fibropurulent exudate. Sterile cultures of the pericardial fluid were not unexpected in view of the extensive antibiotic therapy for over a week prior to paracentesis and surgery. It is our feeling that this case represents a purulent pericarditis secondary to pneumonia, although a benign "nonspecific" or tuberculous pericarditis could presumably have been present. The character of the pericardial fluid and the clinical course, however, would militate against the two latter possibilities.

Summary

A case of subacute purulent pericarditis which was treated by incision and drainage of the pericardium is presented.

An awareness of this complication is stressed because of the dramatic favorable response to adequate surgical therapy.

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Lipoma of the Stomach with Ulceration

Case Report of a Case

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Benign tumors of the stomach are unusual, constituting from 0.5% to 5% of all gastric tumors.[4,7,8,10,15,22] Finesilver [11] reported finding an average of one benign gastric tumor per 7200 roentgen examinations of the stomach. Root [19] found 17 benign gastric tumors in 250,000 hospital admissions, an incidence of 11 per 14,705 admissions. Thompson and Oyster [22] found 66 benign gastric tumors in 20,000 autopsies. Lipomas constitute 2% to 5% of all benign gastric tumors,[8,9,15,22] and several large hospitals have no record of this lesion occurring in their files.

Rumold,[20] in 1941, collected all reported cases of lipoma of the stomach since 1835 and added 1 of his own, bringing the total to 33. In 1946, Scott and Brunschwig [21] added 5 cases from the literature and 1 of their own, bringing the total to 39. Falla Alvarez [2] collected 4 more from the literature and added 1 of his own, making the total 44. Palazzo [16] added 6 personal cases in 1949, bringing the total to 50. Since that time, individual case reports by Culver and Dobrak,[6] Thompson and Oyster,[22] Phelan and Rowan,[17] Badner and Caplan,[3] Cassel and Guccione,[4] and Agey and Ponka [1]; and reports of 2 cases each by Warren and Brandenburg [23] and King and Woelfel [14] bring the total to 60. The present case is the 61st reported in the English literature. No other case was found in the files of this hospital.

Many of the reported cases were incidentally discovered at autopsy and apparently had caused no symptoms during life. A few were found incidentally in the surgical specimen of a stomach removed for other disease. This leaves less than half of the reported cases in which symptoms were significant enough to warrant attention by the patient and physician. The usual symptoms are pain, hemorrhage, digestive complaints, and obstructive signs due to invagination through the pylorus. Radiographic findings are usually indicative of a benign tumor, although no findings are characteristic of this type of tumor and malignancy can seldom be definitely ruled out. Therefore, surgical removal is the treatment of choice when these lesions are discovered radiographically.

Submitted for publication Dec. 27, 1957.

Roswell Park Memorial Institute, Buffalo.

Report of Case

A 58-year-old white housewife was admitted to the hospital in September, 1955, for a hysterectomy for postmenopausal bleeding due to endometrial hyperplasia. She had received external radiation to the uterus in 1938 for menorrhagia. In 1945, and again in June, 1955, dilation and curettage was performed for irregular menses. The admission history revealed that she had "always had a weak stomach," characterized by mild symptoms of indigestion for many years. For one year she had complained of epigastric pain, indigestion, and intolerance to fatty foods. There had been no vomiting, bleeding, or weight loss. She had been a known diabetic for four years, with dietary control, but she had received no insulin. A lower abdominal tumor, pathology unknown, had been removed in 1932.

Physical examination revealed marked obesity and short stature. Her weight was 102.5 kg. B.P. 150/90. The upper jaw was edentulous; the lower teeth were carious. The abdomen was markedly obese. No mass was felt. There was an old lower midline abdominal scar.

X-rays of the upper gastrointestinal tract (Fig. 1) were reported as follows: "A large mass, measuring approximately 6-7 cm. in diameter, is present along the greater curvature aspect of the distal portion of the body of the stomach. The circumference of this mass is smoothly demarcated from the remaining, uninvolved stomach. In the central

Fig. 1.—X-ray of stomach showing rounded lesion with central ulceration.

portion of this mass there is a rounded deposit of barium, measuring approximately 1.5-2 cm. in diameter and representing a central ulcer crater. The presence of a mass having the characteristics described suggests that we are dealing with an intramural lesion, such as a leiomyoma, neurofibroma, or lipoma. One could not exclude with certainty, however, the possibility that this represents a wall lesion with superimposed sarcomatous change, nor could one exclude with any degree of certainty the possibility that this may represent a primary carcinoma of the stomach."

Laboratory findings on admission were within normal limits, with the exception of 4+ sugar in the urine, a positive reaction for acetone, and a trace of albumin. Fasting blood sugar was 212 mg. per 100 cc. Gastric analysis revealed 4+ occult blood in two specimens.

Two weeks of hospitalization was required for diagnostic studies and control of the diabetes with diet and insulin. On Sept. 20, with the patient under general anesthesia, laparotomy was performed through an upper abdominal transverse incision. On the greater curvature of the body of the stomach was a very soft, smooth, disc-shaped mass, 7×7×3 cm., lying within the wall of the stomach, with central ulceration on the mucosal surface. A variant of malrotation of the intestine existed, with complete lack of fixation of the right colon, absence of the ligament of Trietz, and descent of the duodenum on the right side of the abdomen. A large wedge resection of the greater curvature of the stomach was performed, with closure in layers. Postoperatively the patient was placed on prophylactic bishydroxycoumarin (Dicumarol) because of the obesity and the presence of varicose veins. On the ninth postoperative day a superficial wound abscess was drained. Later the same day she developed hematemesis. The bishydroxycoumarin was discontinued, and intravenous vitamin K_1 oxide was administered, with prompt cessation of the bleeding. She was discharged from the hospital on the 16th postoperative day. Follow-up examinations for six months revealed complete relief from gastrointestinal complaints.

Fig. 2.—Gross specimen showing lipoma of stomach, central ulceration, normal adjacent mucosa, and attached omentum.

Fig. 3.—Specimen cut through the center.

Grossly, the specimen (Figs. 2 and 3) consisted of a wedge-shaped segment of stomach, measuring 7×8 cm., with attached omentum. The serosal surface was not unusual. On the mucosal surface was a large round lesion, measuring 7 cm. in greater diameter, in the center of which was an ulcer measuring 1.5 cm. in diameter. The tumor was yellowish in color and grossly resembled fat. Microscopically, the tumor was composed of fat cells. It arose between the submucosa and the muscularis. The ulceration had a base of granulation tissue. Pathological diagnosis: lipoma of the stomach with ulceration.

Summary

Benign tumors of the stomach constitute 0.5% to 5% of all gastric tumors. Lipomas constitute 2% to 5% of benign gastric tumors.

A tabulation of 60 previously reported cases of lipoma of the stomach is presented.

A case of lipoma of the stomach with ulceration is reported. This is the 61st reported case.

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Congenital Atresia of the External Iliac Artery

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Although the surgical literature contains numerous reports on congenital anomalies of the aortic arch and of the pulmonary and splanchnic vessels, few studies have dealt with congenital anomalies of the arteries of the lower extremities. The early anatomical literature contains several descriptions of cadavers with congenital absence of the superficial femoral artery,[1] but we have been unable to find a previous description of congenital atresia of the external iliac artery.

Report of Case

The patient, a white man aged 27, a brickmason, was first admitted to Grady Memorial Hospital in October, 1956, with a two-year history of progressive intermittent claudication involving the left calf. For six months preceding admission, cramps would develop in the left calf after walking one block, or after climbing one flight of stairs. There was no history of trauma, impotence, or surgery. The mother stated that his birth had been uncomplicated and without trauma. There was no history of vascular disease or vascular abnormality in the family. In addition to the usual childhood diseases, he had had scarlet fever at the age of 11 years. For eight years he had had symptoms of duodenal ulcer, the ulcer having been demonstrated by gastrointestinal series in 1954, and again in 1956. He had smoked a package of cigarettes daily for 10 years.

On physical examination, the patient appeared well developed and without evidence of secondary anomalies. Blood pressure in the left arm was 132/76. The skin and hair were normal, including those of the symptomatic, left leg. The peripheral pulses of the upper extremities and the right lower extremity were easily palpable. There was absence of pulsation over the left femoral, popliteal, dorsalis pedis, and posterior tibial arteries. Otherwise, the examination and routine laboratory studies were negative.

The skin temperature of the left leg was 2 to 4 degrees (F) cooler than comparable areas of the right leg. Oscillometric deviations of the right thigh and calf were normal, but were 0 to 1.25 in the left thigh and calf. Translumbar aortography demonstrated patency of the aorta, the renal arteries, the common iliac arteries, the internal iliac arteries, and the right external iliac artery. There was nonfilling of the left external iliac artery (Fig. 1). Intravenous and retrograde pyelograms were normal.

Fig. 1.—Aortogram outlining the right external and internal iliac arteries and the left internal iliac artery. The left internal iliac artery appears to be as large as the right common iliac artery.

At laparotomy, in December, 1956, the abdominal aorta, the common iliac arteries, and the right internal and external iliac arteries were normal. The left internal iliac artery was enlarged. At the origin of the left external iliac artery there was an occlusion, which consisted of an abrupt loss of the lumen (Fig. 2). The artery appeared hypoplastic or constricted throughout the external iliac, common femoral, and superficial femoral artery, the last vessel being explored only to the midthigh. No lumen was present in the hypoplastic artery. The profunda femoris artery was not patent at its origin, but was quite large and patent from its point of junction with the medial and lateral femoral circumflex arteries distally. It ap-

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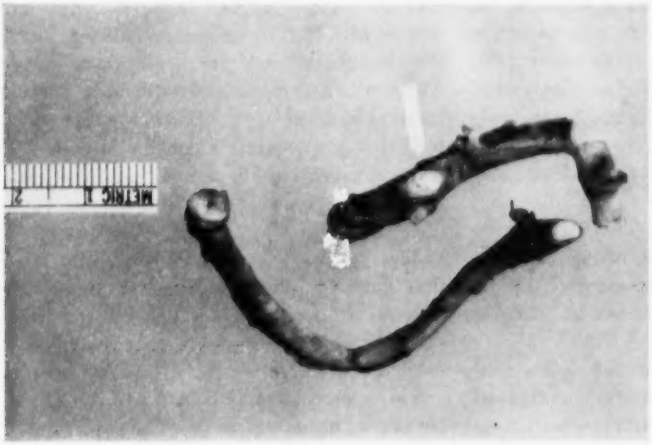

Fig. 2.—Segments of the resected external iliac and femoral arteries. The blind origin of the external iliac artery is shown at the right end of the upper segment. This vessel was resected flush with the common iliac. Cross sections of the artery are shown at the left and in the lower segment. The arrow points to the origin of the profunda femoris artery.

peared to be responsible for the greater part of the blood supply to the left leg, although exploration for the presence of other collaterals, such as a persistent sciatic artery, was not performed. Resection of the left external iliac and common femoral arteries was done, and an arterial homograft was placed end to end between the common iliac and the profunda femoris artery. Owing to tension of the suture lines, it was necessary to splice the graft.

The postoperative course was marked by a series of wound complications and small-bowel obstruction, which required a secondary laparotomy on the seventh postoperative day. An obstructing adhesive band was released. For several days, the temperature of the left foot was cooler than that of the right; thereafter its temperature returned toward normal.

Two months after surgery, the patient was fully ambulatory and working daily as a brickmason. Skin temperature and oscillometric determinations were comparable to those done preoperatively. Intermittent claudication persisted and was considered by the patient to be equal in character and mode of onset to that noted prior to operation.

Microscopic study of serial sections taken longitudinally through the atretic portion of the artery showed a conical constriction of all the mural elements. The lumen was replaced by a diaphragm consisting of intima and subintimal elastic fibers. Beyond the diaphragm, the lumen was replaced by an old, organized, partially recanalized thrombus.

Comment

Evans [2] has shown that the development of the peripheral vascular system is marked first by the progressive formation of functioning capillary-like networks. These networks eventually coalesce to become channels of arterial or venous flow.

In the early embryo, the main artery of the lower extremity is the sciatic, or ischiatic, artery, an artery which passes down the back of the thigh in association with the sciatic nerve. This artery is a branch of the inferior gluteal, which, in turn, is a branch of the internal iliac.

As the femoral artery develops, the embryonic sciatic artery disappears. The popliteal artery remains, however, as a permanent residual of the sciatic artery, to be joined in continuity by the developing femoral artery (Fig. 3). This permanent remnant of the disappearing sciatic artery appears invariable, no instance having been recorded of the congenital absence of the popliteal artery, even though its proximal and distal connection may be quite abnormal.[3]

In the 22 mm. embryo, this embryonic arterial system persists as the popliteal artery and as a network of small arteries in the posterior thigh, which represents the bed of the newly formed deep femoral (profunda femoris) artery.[3] One embryologist described the peroneal artery as being a permanent, distal continuation of the sciatic-popliteal system.[4]

Senior [1] collected from the early anatomical literature the records in which the sciatic (ischiatic) artery had retained its embryonic

form in both limbs of six adult subjects and in one limb of seven others. In these instances, the external iliac artery was patent, the femoral being small and ending either as the profunda or the genicular branches.

Arteriographic study of the patient currently being reported did not include delineation of the vessels distal to the iliac, but the left internal iliac was obviously larger than the right. The sciatic artery could be neither identified nor eliminated. Arterial pulses were not palpable at the left popliteal area or at the left foot.

The congenital nature of this defect cannot be proved beyond the confirmation of the histological picture. Careful questioning elicited no history of trauma or of any other type of vascular disease. The gross appearance of the artery at the site of occlusion was compatible with that of a congenital defect, with the intima lining a smooth, shallow depression over the atretic iliac artery. There was a compensatory dilatation of the internal iliac artery. The microscopic picture strongly suggests a congenital basis for the occlusion, as both intima and subintimal elastic fibers were included in the obstructing diaphragm.

The occluded external iliac artery and that part of the common and superficial femoral arteries which was visualized were easily dissected, seemingly entirely free of periarterial reaction.

This abnormality is believed to have been congenital in nature, the specific defect being a diaphragm occluding the left external iliac artery at its origin. No completely comparable example has been found in the

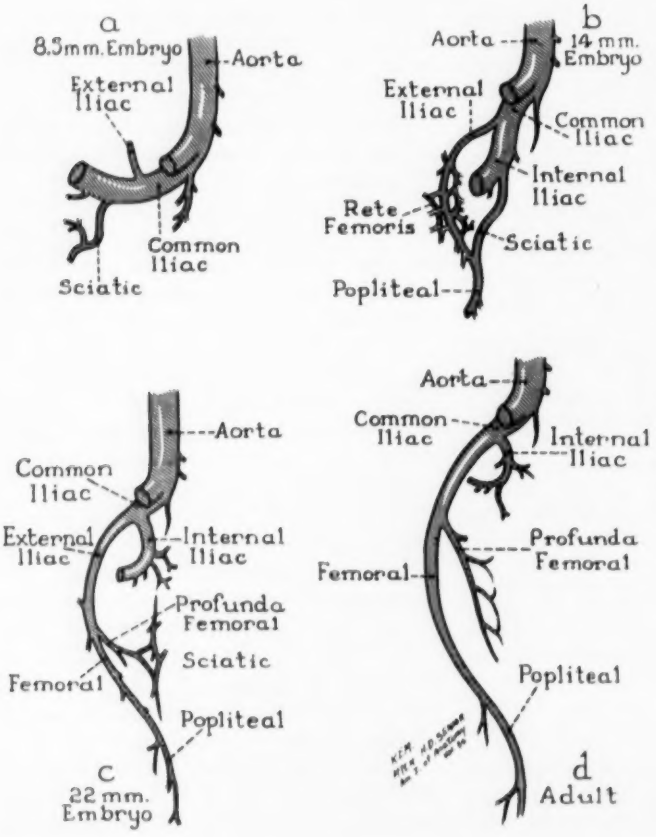

Fig. 3.—Diagram illustrating development of the main arteries of the pelvis and thigh. This shows the persistence of a portion of the sciatic artery as the popliteal. Not shown is the small artery which accompanies the sciatic nerve in the adult.

literature. Treatment has not been successful in this patient. Resection of the defect with reanastomosis would have been a simple technical procedure had it been undertaken prior to the thrombosis in the distal channel.

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Correction

In the article "Arterial Homographs in Immediate Treatment of Severe Injuries to a Major Artery," by Drs. Caldwell J. Gaffney and Willard B. Walker, in the April, 1957, issue (pp. 555-556) the correct address of the authors is St. Louis, Mo., instead of Dayton, Ohio.

Surgery Illustrated

Symposium on Diseases of Gallbladder and Common Bile Duct

Acute Cholecystitis

FRANK GLENN, M.D., New York

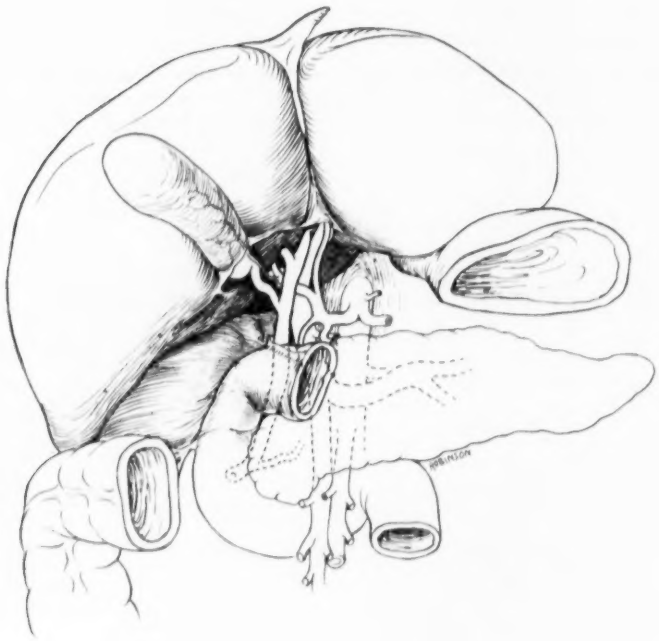

Fig. 1.—Normal anatomical relationships prevail in less than 70% of patients. Alertness to variations and positive identification before division of any structure in this area provide safety from inadvertent injury to blood vessels and the ductal system.

Submitted for publication Nov. 27, 1956.

From the Motion Picture Symposium on Diseases of the Gallbladder and Common Duct given at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956. Two other films in this Symposium material were not presented in time to be included.

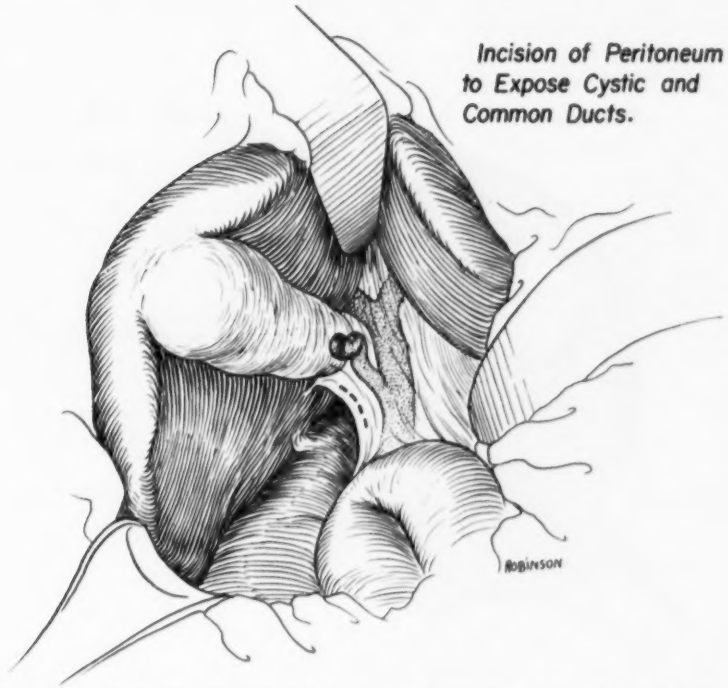

Fig. 2.—An edematous, somewhat rigid, and bulky omentum is adherent to the enlarged, tensely distended, acutely inflamed gallbladder. It is readily reflected away to expose the biliary fossae. After decompressing the distended gallbladder by aspiration with a trocar, the peritoneum is incised to expose the cystic and common ducts.

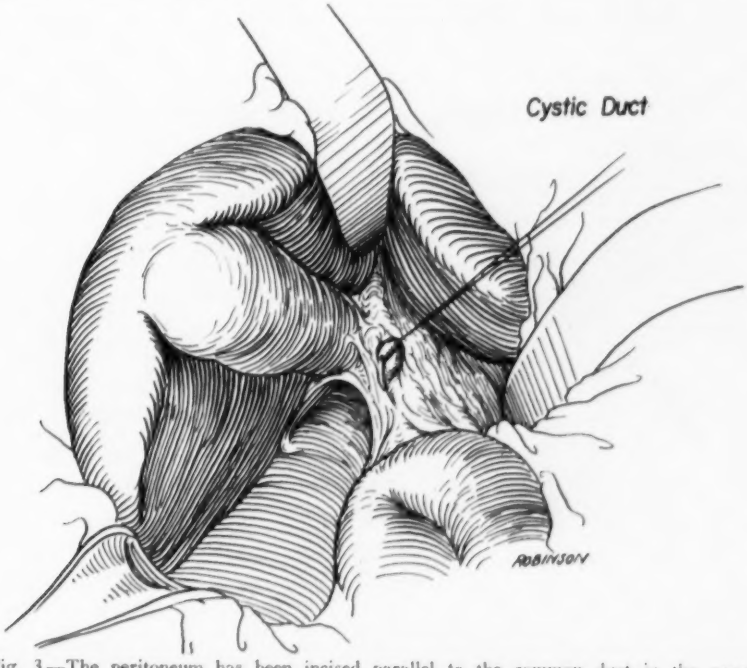

Fig. 3.—The peritoneum has been incised parallel to the common duct in the apparent area of its junction with the cystic duct. The cystic duct is dissected sufficiently to pass a silk ligature about it for identification purposes. The dissection is then extended cephalad and laterally toward the gallbladder wall to expose the cystic artery.

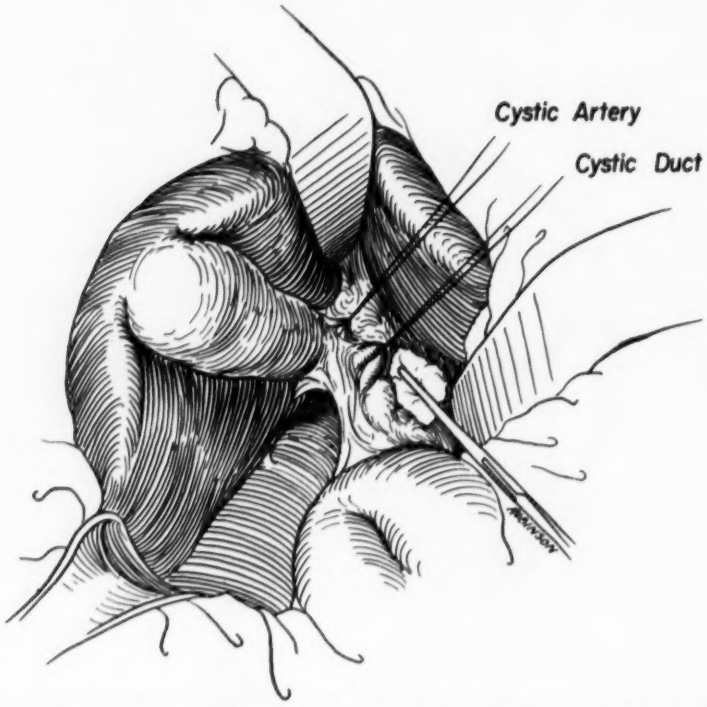

Fig. 4.—The cystic artery is identified and dissected from its entrance into the gallbladder wall to its origin from the right hepatic artery. It is then temporarily ligated by setting one knot in the silk ligature.

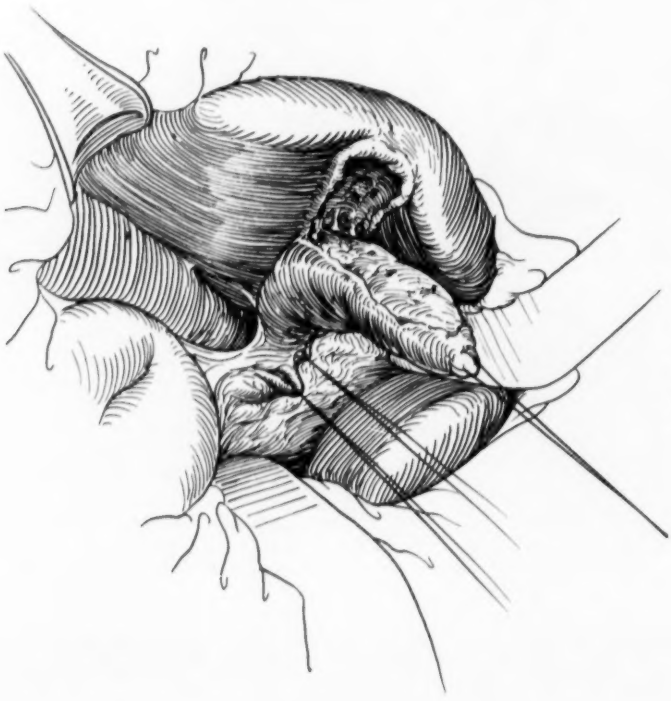

Fig. 5.—The peritoneum over the gallbladder is incised 1 cm. from its junction with the liver, and the gallbladder is dissected from its liver bed from the fundus toward the cystic duct.

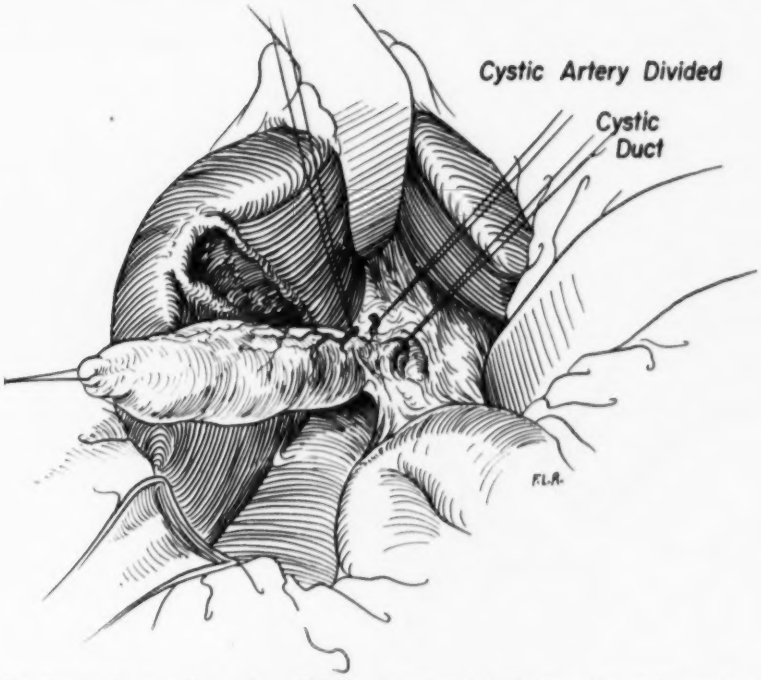

Fig. 6.—As the ampulla of the gallbladder is approached, the branches of the cystic artery as they enter the wall of the gallbladder are divided, and the cystic artery is permanently secured by ligature and transfixing suture.

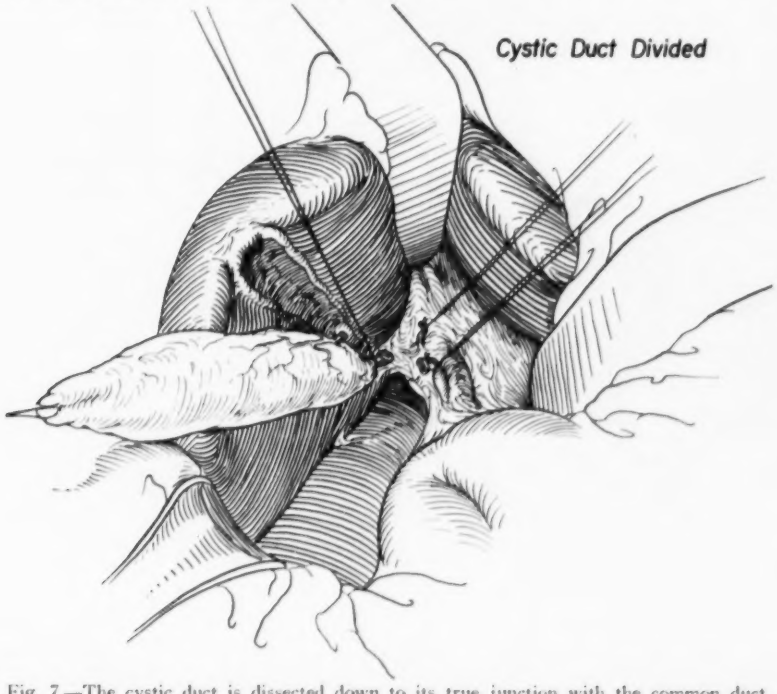

Fig. 7.—The cystic duct is dissected down to its true junction with the common duct. It is secured with ligature of 000 plain absorbable surgical suture U. S. P. 3 mm. from its junction. Just proximal to this is placed a transfixing suture of fine silk and the cystic duct divided, permitting the removal of the gallbladder.

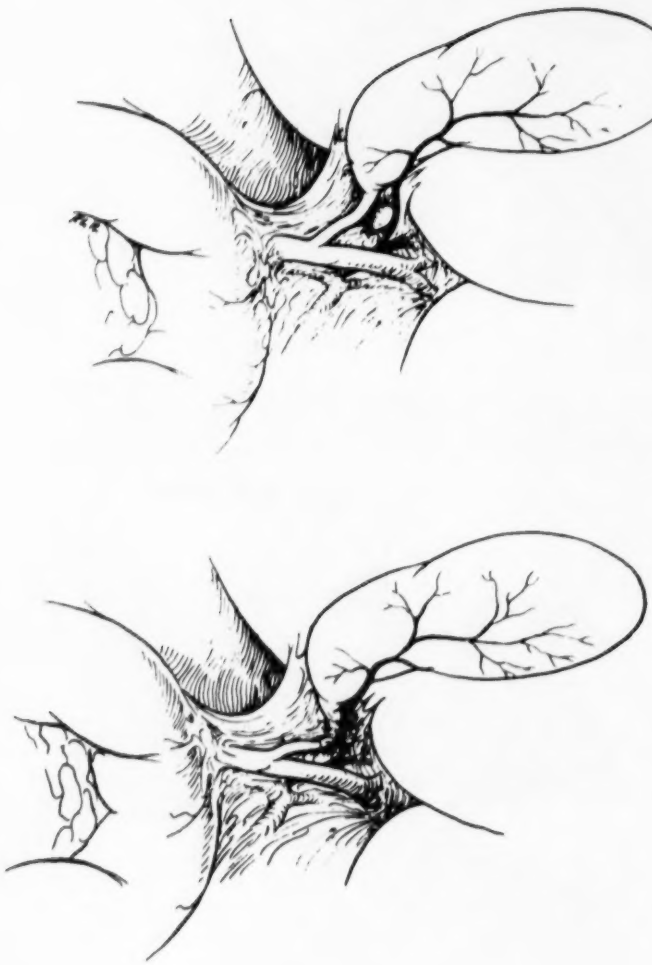

Fig. 8. — In acute cholecystitis the lymph gland commonly located between the cystic artery and the cystic duct is usually enlarged. It may be scarred and contracted, distorting both cystic artery and cystic duct. This may render the separation of these two structures difficult. Care in dissecting in this area is mandatory for safety.

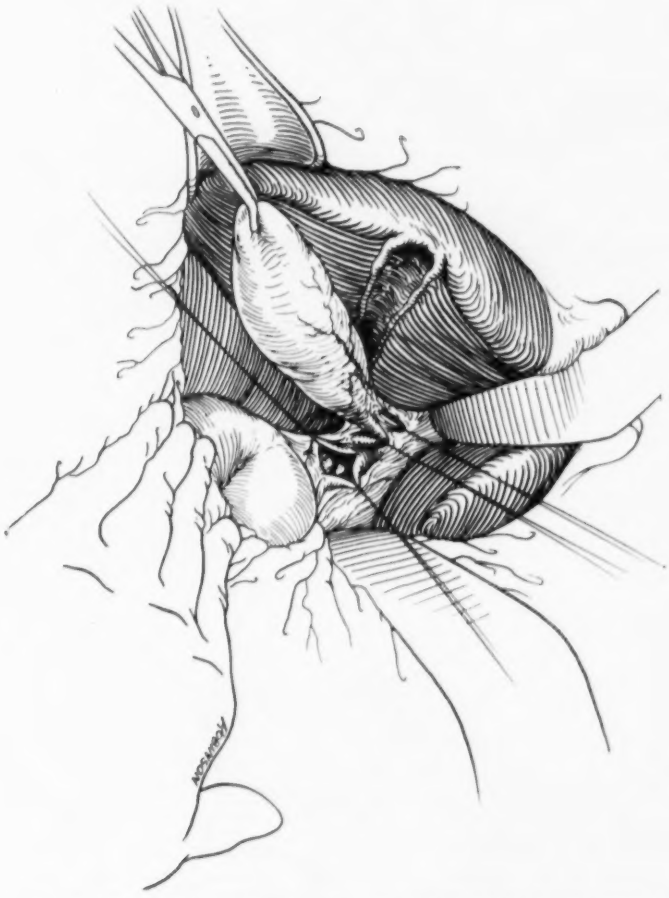

Fig. 9.—The gallbladder has been removed from the fundus downward, exposing the cystic artery and duct. The common duct has been opened by an incision 2 cm. in length extending distally from the level of the cystic duct, revealing choledocholithiasis.

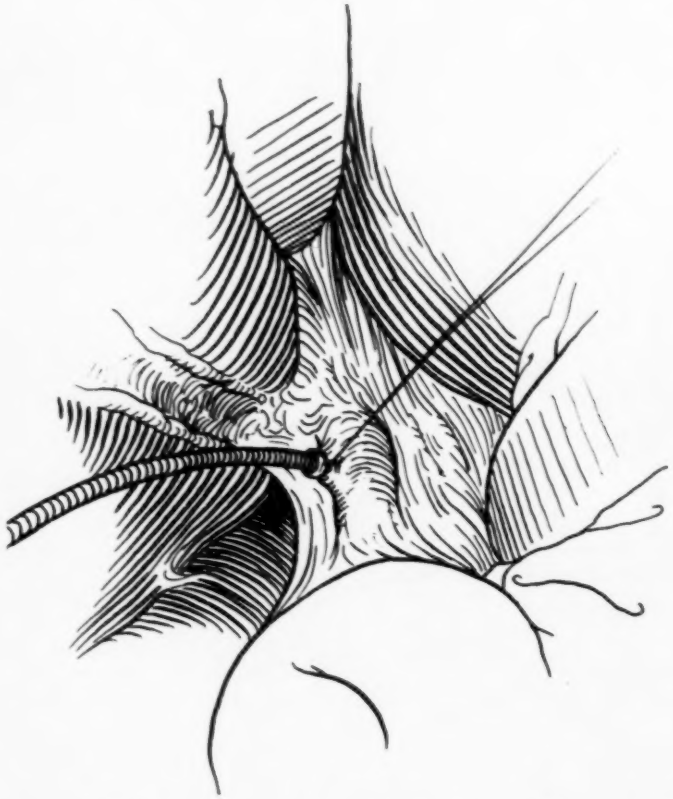

Fig. 10.—If a cholangiogram is to be done, a catheter is inserted into the cystic duct prior to opening the common duct.

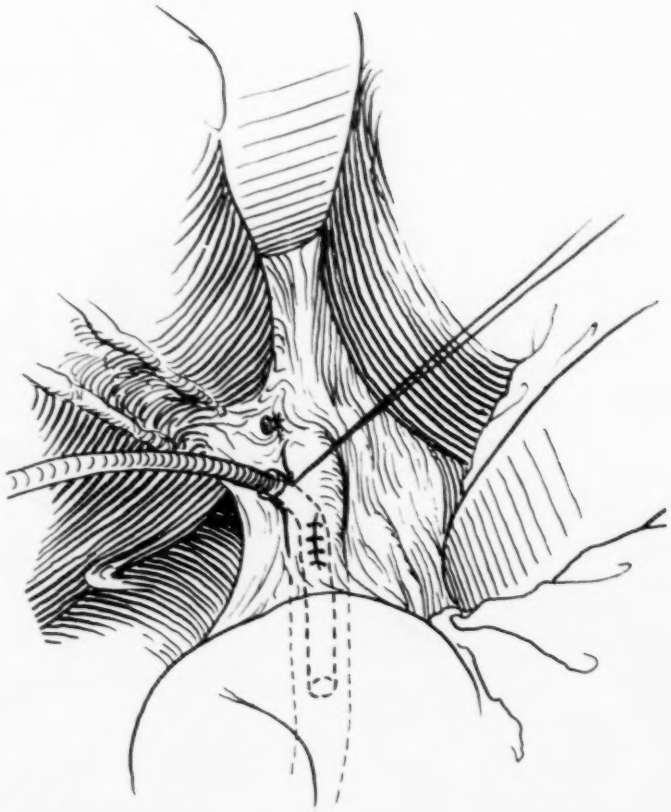

Fig. 11.—Following exploration of the common duct and the removal of stones, the wall of the common duct is reapproximated with interrupted sutures and the catheter brought out through the cystic duct stump as indicated.

Precautions and Errors in Surgery of the Gallbladder and Bile Ducts

WARREN H. COLE, M.D., Chicago

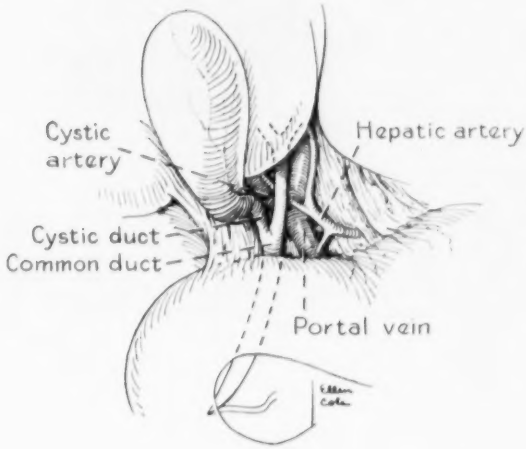

Fig. 1.—NORMAL ANATOMY: Anomalies are so common in the biliary tract that this sketch illustrates a composite of conditions most commonly observed.

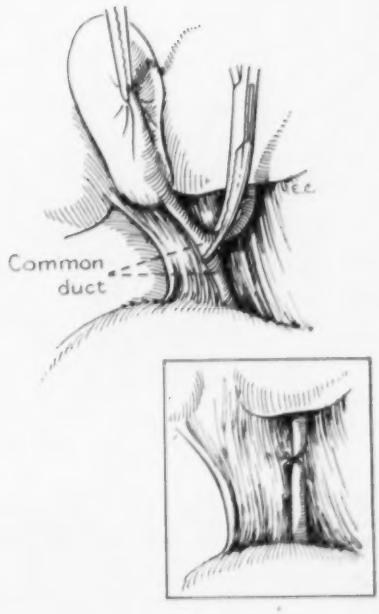

Fig. 2.—ANOMALY: Unusually mobile common duct covered with filmy adhesions (very common). DANGER: If the surgeon is careless and in a hurry, he may clamp the common duct and obstruct it with the ligature, as shown in the insert.

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From the Motion Picture Symposium on Diseases of the Gallbladder and Common Duct given at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956. Two other films in this Symposium material were not presented in time to be included.

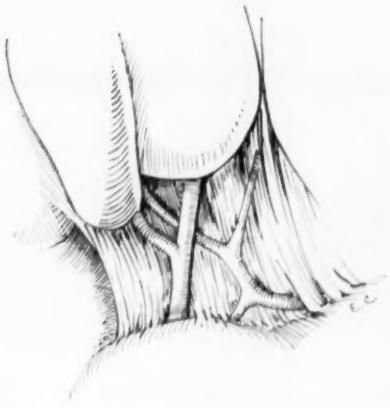

Fig. 3.—ANOMALY: The right hepatic artery proceeds anteriorly from its position under the common duct, coursing forward adjacent to the cystic duct, and enters the liver a few millimeters anteriorly; thus it may resemble the cystic artery (10% to 15% of cases). DANGER: If the surgeon does not recognize this anomaly, he may ligate the right hepatic artery, thinking it is the cystic artery.

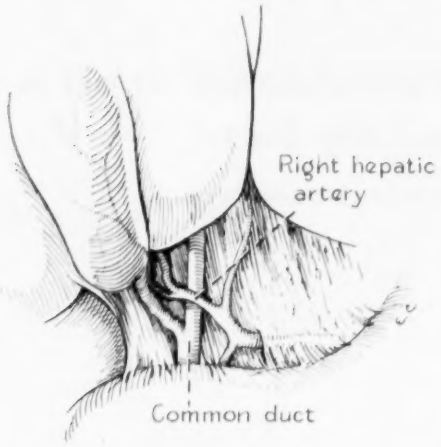

Fig. 4.—ANOMALY: The right hepatic artery crosses anterior to the common duct (present in about 16% of cases). DANGER: If the surgeon does not recognize this anomaly, he may mistake the right hepatic artery for the cystic artery, or damage it while opening the common duct.

Fig. 5.—ANOMALY: Large short cystic duct (common). DANGER: Small stones may drop into the common duct from the gallbladder; also, the common duct may be pinched with the cystic-duct ligature because inadequate cystic duct is available for a safe ligature without extreme care.

Fig. 6.—ANOMALY: An aberrant hepatic duct empties into the gallbladder from the right lobe of the liver (1% to 3% of cases). DANGER: If this duct is not recognized and tied securely, it may leak postoperatively and produce bile peritonitis or give rise to a large collection of bile.

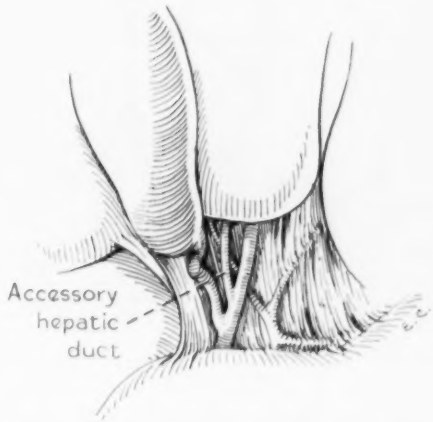

Fig. 7.—ANOMALY: Accessory hepatic duct empties into the common duct (uncommon). DANGER: This duct should not be ligated; it might be the right hepatic duct.

Fig. 8.—ANOMALY: Unusually large Hartmann's pouch lying against the common duct.

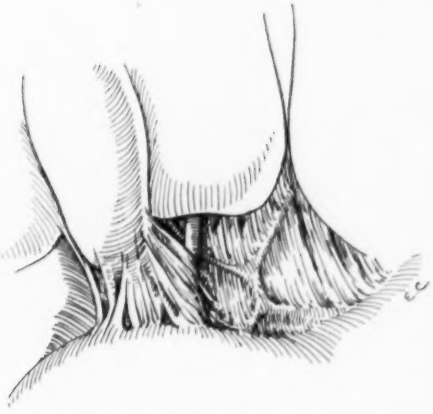

Fig. 9.—DANGER: If adhesions form between a large Hartmann's pouch and the common duct, the latter may be damaged during dissection of the gallbladder from adjacent structures.

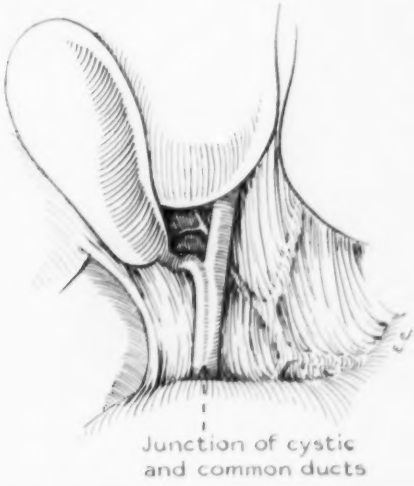

Fig. 10.—ANOMALY: Unusually long cystic duct adherent to the common duct by congenital or inflammatory adhesions.

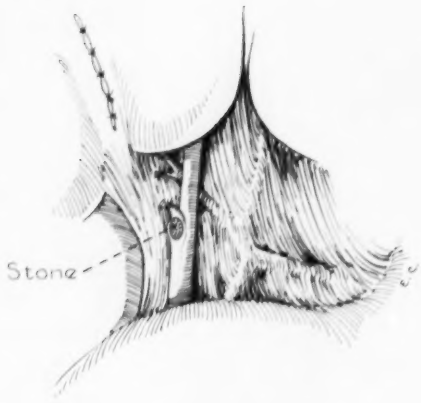

Fig. 11.—DANGER: If the surgeon does not recognize the long cystic duct, he may leave too much; it may contain a stone which may produce symptoms later.

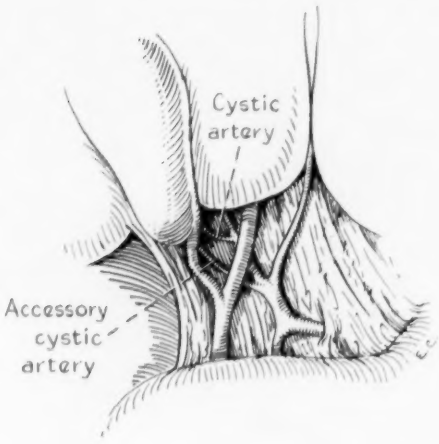

Fig. 12.—ANOMALY: Accessory cystic artery. DANGER: If the surgeon does not recognize the accessory artery, and carelessly cuts it during dissection, serious hemorrhage may result.

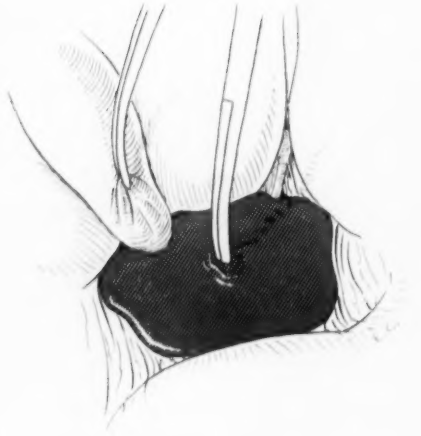

Fig. 13.—ERROR: When profuse hemorrhage develops suddenly in the depth of the wound during dissection, the surgeon may erroneously start stabbing in the wound to clamp the bleeding point, and grasp part of the common duct with the clamp.

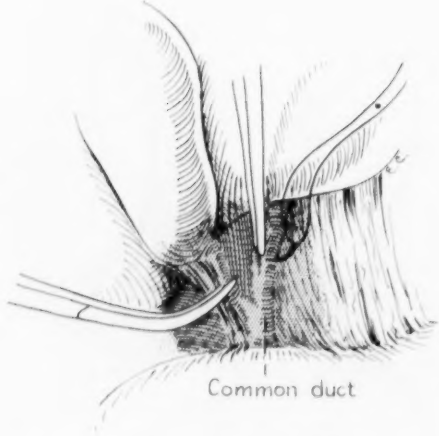

Fig. 14.—ERROR: The surgeon tries to ligate the bleeding point in a field obscure because it is blood-stained, or the anatomy is incompletely identified. Ligation of a large segment of tissue, especially if a needle is used, may endanger the common duct.

Fig. 15.—CORRECT METHOD OF CONTROLLING SEVERE HEMORRHAGE: Rather than clamp the bleeding point blindly, one should insert the index finger into the foramen of Winslow and compress the hepatic artery between the index finger and thumb.

Fig. 16.—ERROR: The cystic artery has been ligated so close to the common duct that infection, with foreign-body reaction from the suture, may give rise to sufficient fibrosis to result in a stricture.

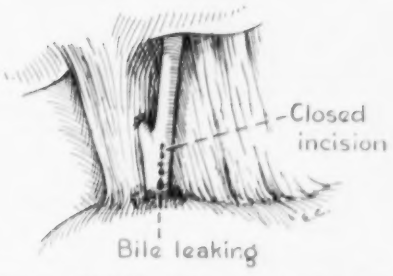

Fig. 17.—ERROR: When a choledochotomy is done for stones, closure without T-tube drainage may result in leakage of bile from the suture line, with production of bile peritonitis or localized collection of bile.

Fig. 18.—LEAKAGE OF BILE: Bile may accumulate in the peritoneal cavity from an unligated aberrant duct, from the cystic-duct stump, or from a choledochotomy wound closed without drainage, and bile peritonitis may develop (fatal unless drained); if the amount of bile is small (and located over the common duct), an inflammatory reaction (with or without an abscess) may produce enough damage to result in a stricture.

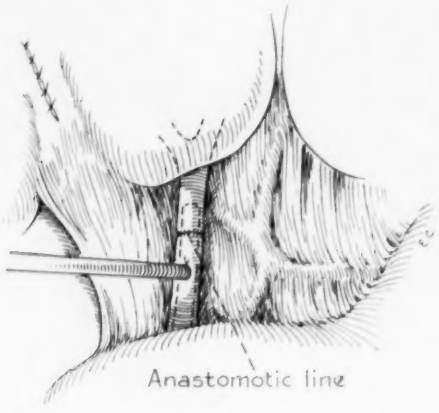

Fig. 19.—REPAIR OF A LOCALIZED STRICTURE: If the two ends of the common duct can be approximated without tension, an end-to-end anastomosis should be performed with a T-tube prosthesis brought out above or below the suture line, not through it; in such a case it is usually advisable to leave the tube in place for 9 or 10 months.

Fig. 20.—REPAIR OF A DIFFUSE STRICTURE: If the lower end of the common duct cannot be found, I prefer use of a Roux Y-arm of jejunum, utilizing no T-tube splint if the stoma is large and minimal inflammation is present in the duct. If the stoma is small and much inflammation present in the duct, a T-tube should be used and left in place for 9 or 10 months. Alternate techniques consist of choledochoduodenostomy and use of a loop of jejunum, but I prefer the Roux Y-arm.

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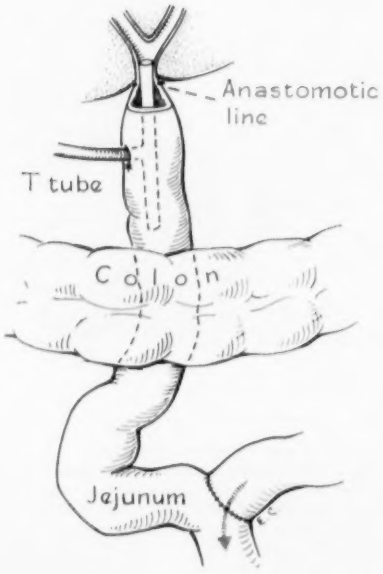

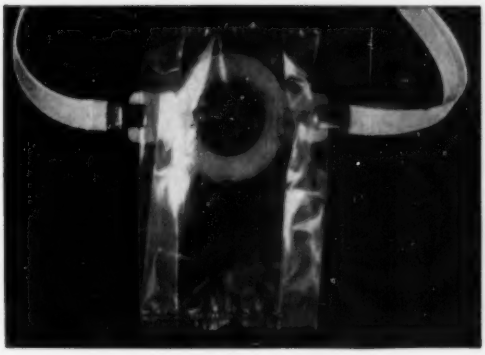

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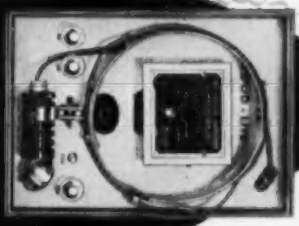

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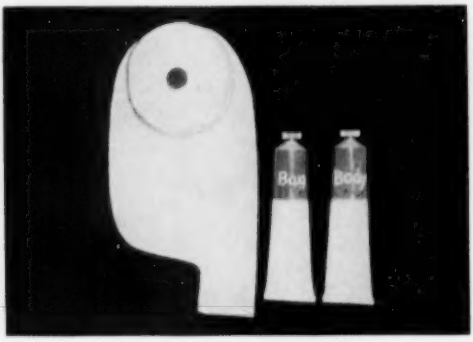

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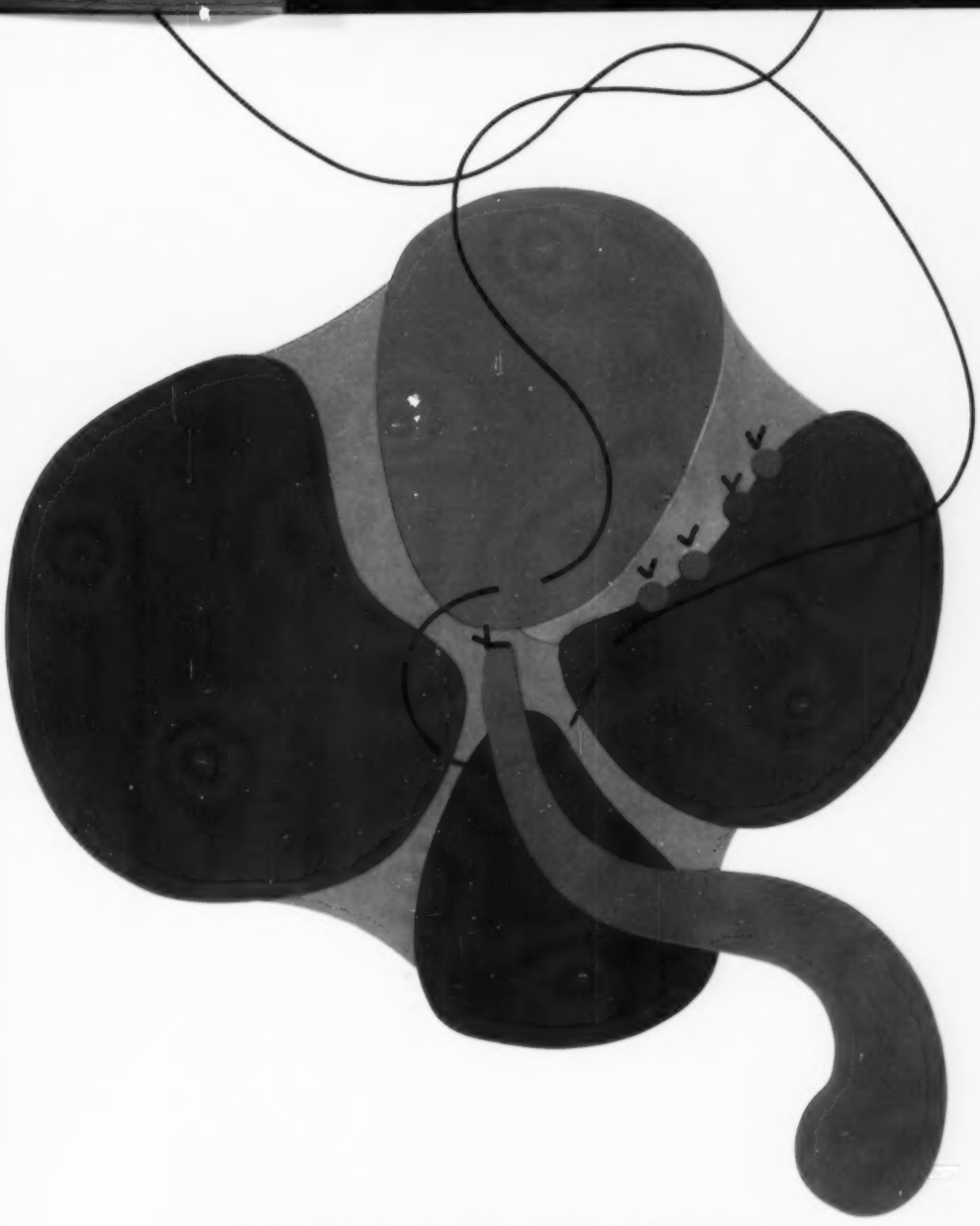

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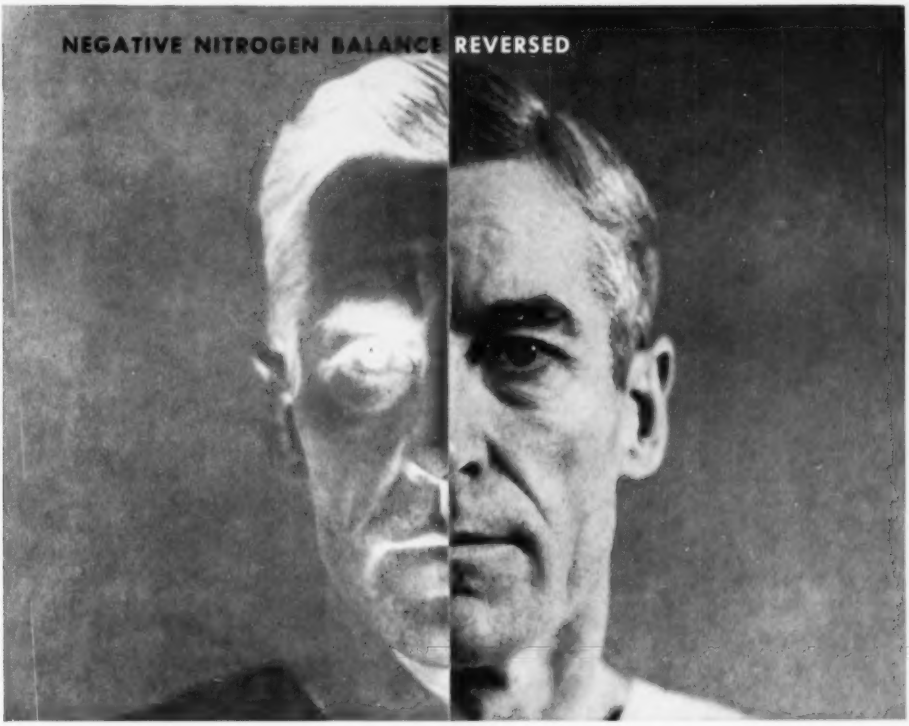

Nilevar®

stimulates protein synthesis,
corrects negative nitrogen balance

Increased nitrogen loss, with resulting negative nitrogen balance, occurs in infection, trauma, major surgery, extensive burns, certain endocrine disorders and starvation and emaciation syndromes. The intrinsic control of protein metabolism is lost and a protein "catabolic state" occurs. A patient requiring more than ten days of bedrest usually has had sufficient metabolic insult[1] to precipitate such a "catabolic" phase.

Nilevar (brand of norethandrolone) has been used in patients with varied conditions including hyperthyroidism, poliomyelitis, aplastic anemia, glomerulonephritis, anorexia nervosa and postoperative protein depletion. The patients gained weight and felt better. It was concluded[2] that "the drug certainly caused a reversal of rather recalcitrant or progressive catabolic patterns of disease."

Nilevar is unique among anabolic steroids in that androgenic side action is minimal or absent.

The suggested adult dosage is three to five tablets (30 to 50 mg.) daily. For children 1.5 mg. per kilogram of weight is recommended.

G. D. Searle & Co., Chicago 80, Illinois.
Research in the Service of Medicine.

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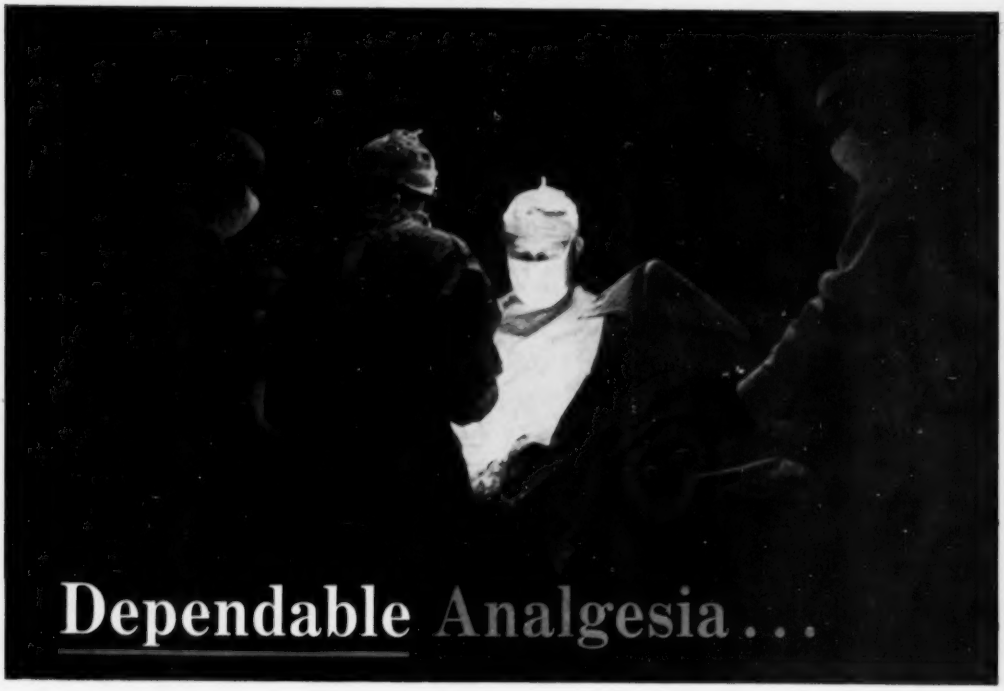
1. Axelrod, A. E.; Beaton, J. R.; Cannon, P. R., and others: Symposium on Protein Metabolism, New York, The National Vitamin Foundation, Incorporated, (March) 1954, p. 100.

2. Proceedings of a Conference on the Clinical Use of Anabolic Agents, Chicago, Illinois, G. D. Searle & Co., April 9, 1956, pp. 32-35.

SEARLE



PROFOUND • PROLONGED • CONTROLLED

with Pontocaine®

hydrochloride

SADDLE BLOCK

0.2% Pontocaine HCl in dextrose (hyperbaric) ampuls of 2 cc. (4 mg.) Also "Niphanoid"® (instantly soluble dry form) and 1% solution in saline (isobaric)

SPINAL

HIGH
MEDIUM
LOW

0.3% Pontocaine HCl in dextrose (hyperbaric) ampuls of 5 cc. (15 mg.)

"Niphanoid," ampuls of 10, 15 and 20 mg.

1% solution (in saline) 2 cc. (20 mg.)

NERVE BLOCK AND INFILTRATION

0.15% solution, vials of 100 cc.

"Niphanoid," ampuls of 250 mg.

Winthrop **LABORATORIES**
NEW YORK 18, N. Y. • WINDSOR, ONT.

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